REMARKS/ARGUMENTS

Reconsideration of this application and entry of the foregoing amendments are respectfully requested.

The Examiner's objection to the specification is noted but the basis for that objection is not understood and clarification is requested. The pages/lines referenced by the Examiner have been reviewed but no words have been found to be missing and the text is legible. The indicated pages of the application in the Image File Wrapper (accessible through PAIR) also appear to be in good order. Nonetheless, submitted herewith are further copies of pages 2, 3, 4, 5, 7, 8, 9 11 and 13 – it is requested that they be substituted for the corresponding pages as filed, should the Examiner view such substitution to be necessary. The text of the pages provided herewith is the same as the text of the corresponding pages of the PCT application as filed. Accordingly, substitution of the attached copies for the corresponding pages as filed would not add new matter. In view of the above, the Examiner is requested to withdraw the objection or to more clearly explain the basis for his concern.

Claims 1-30 have been cancelled without prejudice and new claims 31-55 have been added. New claims 31-53 correspond to now cancelled claims 1-5, 7, 9, 10, 12-18, 21-25 and 27-29, respectively.

Claim 5 (corresponding to new claim 35) does not include a superfluous "in". Withdrawal of the objection to prior claim 5 is, therefore, requested.

Claims 23, 24, 27 and 28 stand rejected under 35 USC 112, first paragraph, as allegedly being non-enabled. Withdrawal of the rejection is believed to be in order for the reasons that follow.

Claims 23, 24, 27 and 28 have been re-presented as new claims 48, 49, 51 and 52, respectively. The new claims include a positive recitation of the process steps. Support for the recited steps can be found in the description of the relevant process steps in the specification. For example, the specification at pages 14 to 19 adequately describes General Methods 4, 7, 14, 15, 16 and 22 which correlate to the process steps a, b, and c as defined in claims 48, 49, 51 and 52.

In view of the above, reconsideration and withdrawal of the rejection are requested.

Claims 1-30 stand rejected under 35 USC 112, first paragraph, as allegedly being non-enabled. Withdrawal of the rejection is submitted to be in order for the reasons that follow.

The Examiner contends that the scope of groups heteroalkyl, heteroarylacyl, heteroaryloxy, aminoheteroaryl, thioheteroaryl, and heteroarylalkyl is not adequately enabled. While in no way agreeing the Examiner, the claims have been revised to additionally conform the claims with the disclosure. Support for the revisions can be found throughout the application, including in the examples.

More specifically:

(i) New claim 31 further defines the group W as selected from the groups (a) to (g). This revision relates to the scope of the terms "hetero", "aryl" and "alkyl" in moieties such as alkyl, heteroaryl and heteroalkyl;

(ii) New claim 31 incorporates the definitions of N(Z)Y and N(T)Y into one as N(Z)Y in order to simplify the definitions in the claim; and

(iii) New claim 31 incorporates definitions of W, X1 and X2 as W in order to simplify the definitions in the claim.

While support for these revisions can be found throughout the application, particular attention is directed to:

a) R2a in tables 1 & 2 and R1g and R2c in table 3 for "alkyl"
R2b in table 1 & 2 and R2d in table 3 for "substituted alkyl"

c) R1d; R1i and R2d in tables 1 & 2 and R1m, R2e, R3i; R3m; R3q, R3s, R3t, R3u, R3v, R3y and R3z in table 3 for "heteroalkyl"

d) R3j, R3k, R3l; R3u in table 3 and compounds 469, 470, 471 and 472 as described on page 72 for the term substituted and unsubstituted "monocyclic or bicyclic aryl";

e) R3a, R3c, R3e; R3f and R33 in table 3 for the term substituted and unsubstituted "monocyclic or bicyclic heteroaryl",

f) R3b, R3g, R3u; in table 3 and R2a, R3b, R3c and R3d in table 4 for the term substituted and unsubstituted "arylalkyl",

g) R3c, R3f and R33 in table 3 for the term substituted and unsubstituted "heteroarylalkyl".

Applicants have provided synthetic methods that are broadly applicable to the compounds within the definitions of new claim 31. Applicants respectfully submit that one skilled in the art could readily prepare compounds as defined in claim 31 comprising the groups alkyl, alkenyl, alkynyl, heteroalkyl, monocyclic or bicyclic aryl,

monocyclic or bicyclic heteroaryl, arylalkyl, and heteroarylalkyl, with or without substituents as defined in new claim 35, without undue experimentation. All of the appended groups on oxygen (i.e., the OW moieties) can be formed by simple alkylation reactions that are extensively exemplified. A very wide range (many 100's if not 1000's) of organic halides suitable for use in alkylation reactions are available commercially. When the group is appended to nitrogen (-N(Z)Y), the Z groups are introduced through a simple acylation reaction that is extensively exemplified. Many thousands of organic carboxylic acids, including a wide range of heterocyclic carboxylates, are commercially available for use in such acylations on nitrogen to provide compounds of the invention. Thus, Applicants submit that one skilled in the art could readily prepare compounds commensurate with the scope of claim 31 based on the teachings of the subject application.

The claims have been further revised to specifically define the scope of the term "hetero" which is limited to the conventional meaning, that being O, S and N atoms only.

The Examiner further contends that there is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since "they are so structurally dissimilar as to be chemically non-equivalent".

Applicants respectfully submit that structural dissimilarity and chemical non-equivalence is an object of the instant invention. The instant application seeks to provide compounds that are peptidomimetics and that explore chemical diversity. Compounds of the invention are expected to exhibit varied biological properties over a

range of receptors. Indeed, the compounds of the instant invention were not designed so as to exhibit the same activities but rather, preferably, a range of activities.

Reconsideration and withdrawal of the rejection are requested.

Claims 1-30 stand rejected under 112, second paragraph, as being indefinite. Withdrawal of the rejection is submitted to be in order in view of the claim revisions discussed immediately above in connection with the rejection of claims 1-30 based on an alleged lack of enablement and further in view of the comments offered immediately above in response to that rejection, those comments being incorporated herein by reference. Reconsideration is requested.

Claims 23, 24, 27 and 28 stand rejected under 35 USC 112, second paragraph, as allegedly being indefinite. Withdrawal of the rejection is submitted to be in order in view of the above-noted revision of the claims as new claims 48, 49, 51 and 52 which recite process steps. Reconsideration is requested.

Claims 3 and 29 stand rejected (apparently under 35 USC 112, second paragraph) because recited limitations do not find antecedent basis in claim 1. Claim 31 incorporates the limitations of prior claim 3 wherein the groups Z and Y may combine with N in N(Z)Y to form a ring and claim 29 has been revised appropriately as new claim 53. Accordingly, withdrawal of the rejection is requested.

Claim 11 stands rejected under 35 USC 112, second paragraph, as allegedly being indefinite. Cancellation of the claim renders the rejection moot.

Claim 28 stands rejected under 35 USC 112, second paragraph, as allegedly being indefinite. New claim 52 does not include the term 'derivatised". The term has been deleted merely to advance prosecution, not because Applicants agree with the

Examiner's position. On the contrary, Applicants submit that one of ordinary skill would readily appreciate the scope and meaning of the term "derivatised polystyrene". Withdrawal of the rejection is clearly in order and same is requested.

Claims 1-30 stand rejected under 35 USC 103 as allegedly being obvious over Aoki et al (USP 5,719,291) and Hirschmann et al (USP 6,197,963. Withdrawal of the rejection is submitted to be in order for the reasons that follow.

As Applicants understand it, the Examiner does not contend that either Aoki et al or Hirschmann et al, alone or in combination, teach or would have suggested the preparation of compounds of the instant invention where n=0. As Applicants further understand it, the Examiner also does not contend that the cited art teaches or would have suggested the preparation of compounds of the instant invention where n=1 and R1 = N(Z)Y. What appears to be at issue is the construction defined as n=1 and R1=H and Applicants offer the following comments with respect thereto.

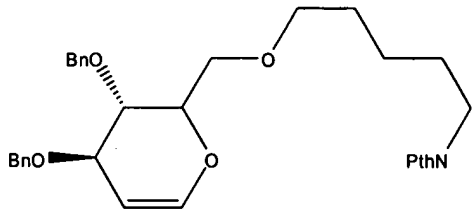
The Examiner remarks that Hirschmann et al teach pyran compounds corresponding to those claimed wherein, for example, R1 is OCH_3, R5 is an amine. Applicants respectfully submit that compounds in which R1 is OCH3 or, indeed, an O-linked derivative are not pyran compounds but rather pyranose compounds and fall outside the scope of the instant invention which limits R1 to either H or N(Z)Y. Applicants submit that there is a very large difference both in preparative chemistry and properties between pyranose compounds and tetrahydro-2H-pyran's of the instant invention.

Hirschman et al describe a large number of compounds. Those based on carbohydrates are detailed in Attachment I for clarity. Applicants point out that of all of

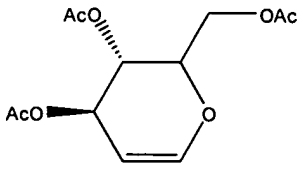
the compounds disclosed by Hirschmann et al, only five compounds have a hydrogen at the anomeric position, i.e., are pyran like molecules. These are compound III-34 of example 11 AG (page 91 line 56) and the simple glycals of examples 25 to 28 (page 110 line 25 to page 111 line 55) all shown below.

None of these compounds falls within the scope of the claims as now presented nor are they obviously convertible to compounds of the instant invention. Apart from the obvious double bond which is outside the scope of the instant invention, the compounds of Hirschmann et al do not meet the criteria that one of the R groups must be OW; one of the R groups must be OH; one of the R groups must be N(Z)Y; and the OW groups must be different.

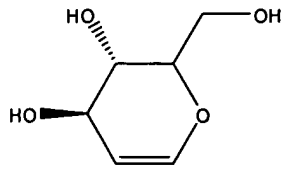
Example 11 AG. III-34



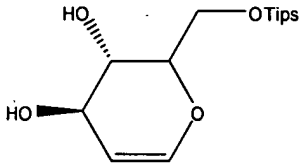
Example 25 compound IV-13



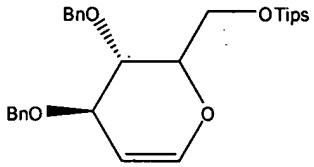
Example 26 compound IV-14



Example 27 compound IV-15



Example 28 compound IV-16



The Examiner remarks that as the substituents of Hirschmann et al are of comparable scope to those recited in the claims any differences would have been obvious to one of ordinary skill in the art due to the close structural relationship of the compounds. Applicants respectfully disagree.

The instant invention relates to monosaccharide derivatives, specifically, wherein R1 is selected from the group consisting of hydrogen or N(Z)Y. The instant invention is based on the premise that when R1 is N(Z)Y, Y is an N-acyl type group, and one other

of R2, R3, R4 and R5 is also N(Z)Y, and the other of the groups R2, R3, R4 and R5 are independently selected from OH, OW and N(Z)Y, wherein the OW groups when present are different. Hence, the instant invention provides a unique combination of moieties not taught by or suggested by Hirschmann et al.

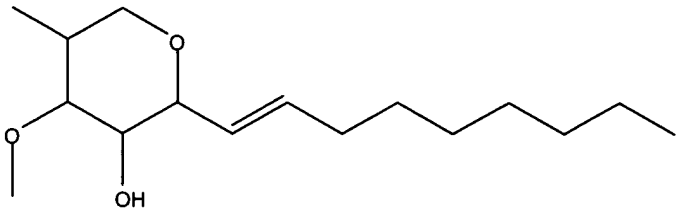
Clearly, the compounds of Hirschmann et al are distinct from those recited in the present claims. Hirschmann et al does not teach nor would it have suggested N-acylated compounds and wherein the OW groups are different as defined according to the instant claims. Furthermore, Hirschmann et al would not have motivated one of ordinary skill to prepare compounds according to the instant invention nor does Hirschmann et al provide methods suitable for the preparation of the compounds of the instant invention.

The Examiner remarks that Aoki et al teaches pyran compounds corresponding to the claimed compounds where R1 is H.

Aoki et al contains a large number of example compounds both of the pyran and cyclohexane scaffold varieties. A listing of all the compounds of the pyran scaffold disclosed in Aoki et al is provided in Attachment II.

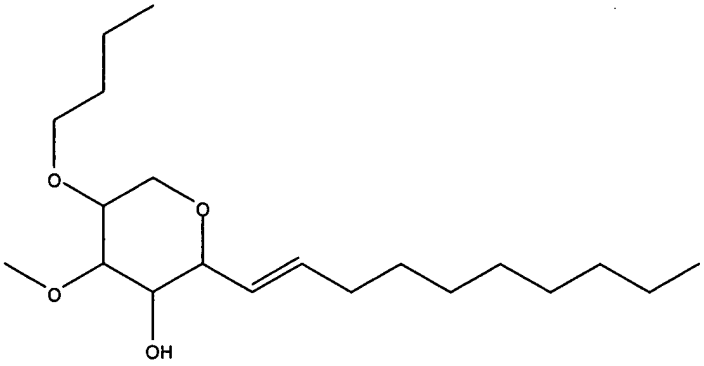
The majority of pyran compounds disclosed by Aoki et al fall into 3 groups:

1. 5-alkyl-4-alkoxy-3-hydroxy-2-alkyl pyrans and derivatives thereof as exemplified by



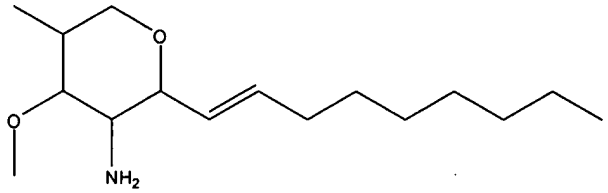
4-methoxy-5-methyl-2-[(E)-1-nonenyl]-tetrahydro-2H-pyran-3-ol

2. 5-alkoxy-4-alkoxy-3-hydroxy-2-alkyl pyrans and derivatives thereof as exemplified by



5-butoxy-4-methoxy-2-[(E)decenyl]tetrahydro-2H-pyran-3-ol

3. 5-alkyl-4-alkoxy-3-amino-2-alkyl pyrans and derivatives thereof as exemplified by



4-methoxy-5-methyl-2-[(E)-1-nonenyl]tetrahydro-2H-pyran-3-amine

None of these groups of compounds fall within the scope of the instant claims since each of these groups of molecules has at its core at least one, and generally two, moieties attached to the pyran ring by a c-c bond. In examples 1 and 3 above, the methyl groups at position 5 are directly attached to the pyran ring, while the nonenyl moieties in all 3 examples are directly attached to the pyran ring.

The methods detailed in the specification of Aoki et al are directed to making such compounds and would not have led the skilled person to compounds of the instant invention.

Applicants' claims require that at least one of the positions R2 to R5 be OH; that at least one of the positions R2 to R5 be OW; that at least one of the positions R2 to R4 be N(Z)Y and that if two OW groups are present, each instance of W is different.

None of the compounds of Aoki et al fulfil these requirements nor is there any teaching in the citation of how such compounds could be prepared. Furthermore, the reference would not have motivated one to prepare such compounds.

It will be clear from the foregoing that neither Aoki et al nor Hirschmann et al, taken alone or in combination, could have suggested the claimed compounds. Accordingly, reconsideration and withdrawal of the rejection are requested.

This application is submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

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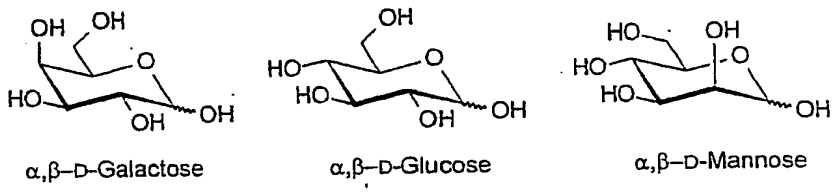


Fig. 1

The first example of a combinatorial approach employing carbohydrate chemistry, was a symposium report on the design and synthesis of a peptidomimetic using a glucose scaffold in the early 1990's[1]. The results, revealed that the glucose based structures designed as mimetics of a potent somatostatin (SRIF) agonist acted as agonists at low concentration, and at high concentration became the first known antagonists of SRIF. Although hardly the production of a library, the results were unique.

Continuing in part the work commenced in the early 1990's, Nicolaou and co-workers began developing carbohydrate based peptido-mimetics targeting integrins. Many integrins recognize an Arg-Gly-Asp (RGD) sequence in ligands such as fibronectin, vitronectin and fibrinogen, each binding with different affinities to the individual integrin receptors. Through a process of rational design a number of carbohydrate based RGD mimetics were synthesized. The chemical synthesis of nine different compounds by this group with very few common intermediates required a considerable amount of chemical effort. It was evident from such results, that in order to generate a number of different structures in a facile manner new chemistries needed to be developed to streamline and enable what at this stage was unfortunately a protracted and arduous methodology.

Since 1998 researchers in the group of Kunz[2] have been developing a number of carbohydrate building blocks with a similar purpose in mind. In general the building blocks that they have developed are coupled to a solid support to effect the desired chemical transformations. The chemistry developed can be employed to achieve, like the work of Hirschmann and co-

workers[3], the introduction of peptidomimetic side chains to carbohydrate scaffolds in an effort to produce glyco-based mimetics of cyclic peptides. Admittedly, with the chemistry they have developed, there are inherent limitations in the types of functional groups that they are able to introduce and the range of stereoisomeric building blocks that they are able to employ.

It is now becoming reasonably established in the art that relates to the solid phase production of combinatorial carbohydrate based libraries, that one of five protecting groups on a carbohydrate scaffold is a protecting group modified as a linker, so as to allow coupling of the block to a solid support. The strategy that then follows is simple, remove a protecting group and effect coupling at the freed functionality with a peptidomimetic or other reagent. Remove another protecting group and couple with the next reagent, and so on.

Following this generally accepted principle, a system has been developed that allows the chemical synthesis of highly structurally and functionally diverse derivatised carbohydrate and tetrahydropyran structures, of both natural and unnatural origin. The diversity accessible is particularly augmented by the juxtaposition of both structural and functional aspects of the molecules. In order to access a wide range of diverse structures, stereo-center inversion chemistry is required, so as to achieve non-naturally occurring and hard to get sugars in a facile manner. Other chemistries are also required that provide unnatural deoxy or deoxy amino derivative which impart greater structural stability to the drug-like target molecules. With a suite of reagents to effect a suitable range of chemistries on a solid support, allowing such things as; wide functional diversity, highly conserved intermediates, a limited number of common building block to be required, and with suitable chemistry to allow access to unusual carbohydrate stereo-representations and including access to deoxy and deoxy amino analogues, a methodology is then established that can create focused libraries for a known target, or alternatively diversity libraries for unknown targets for random screening.

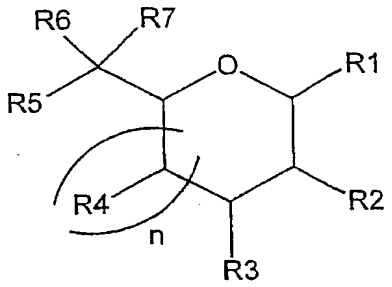
Many of the traditional methods of carbohydrate synthesis have proved to be unsuitable to a combinatorial approach, particularly because modern high-throughput synthetic systems require that procedures to be readily automatable. The compounds and processes described herein are particularly suited to the solid and solution phase combinatorial synthesis of carbohydrate-based libraries, and are amenable to automation. The methods of the invention yield common intermediates that are suitably functionalized to provide diversity in the structure of the compounds so generated. In this way the technology described can produce many and varied compounds around the basic structure shown in Figure 1. Using this method, it is possible to introduce varied functionality in order to modulate both the biological activity and pharmacological properties of the compounds generated.

Thus the compounds and methods disclosed herein provide the ability to produce random or focused combinatorial-type libraries for the discovery of other novel drug or drug-like compounds, or compounds with other useful properties in an industrially practical manner.

It will be clearly understood that, although a number of prior art publications are referred to herein, this reference does not constitute an admission that any of these documents forms part of the common general knowledge in the art, in Australia or in any other country.

SUMMARY OF THE INVENTION

In a first aspect, the invention provides a compound of formula I



formula I

Wherein,

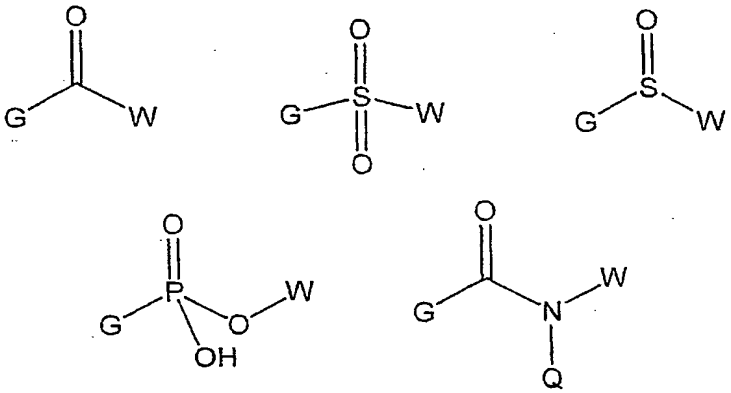
n is 0 or 1; the ring may be of any configuration and the anomeric center may be of either the α or β configuration;

R6 and R7 are hydrogen, or together form a carbonyl oxygen;

R1 is selected from the group consisting of hydrogen; -N(Z)Y and -C(Z)Y wherein;

When R1 is –N(Z)Y, then:

Y is selected from hydrogen, or the following, where G denotes the point of connection to the nitrogen atom in N(Y)Z;



include but are not limited to OH, NO, NO_2, NH_2, N_3, halogen, CF_3, CHF_2, CH_2F, nitrile, alkoxy, aryloxy, amidine, guanidiniums, carboxylic acid, carboxylic acid ester, carboxylic acid amide, aryl, cycloalkyl, heteroalkyl, heteroaryl, aminoalkyl, aminodialkyl, aminotrialkyl, aminoacyl, carbonyl, substituted or unsubstituted imine, sulfate, sulfonamide, phosphate, phosphoramide, hydrazide, hydroxamate, hydroxamic acid;, heteroaryloxy, aminoalkyl, aminoaryl, aminoheteroaryl, thioalkyl, thioaryl or thioheteroaryl, which may optionally be further substituted.

Suitably, When R1 is H, at least two of the groups R2, R3, R4 and R5 are selected from the group consisting of –OX2 or -N(T)Y, and the others are independently selected from hydrogen, -OH, -OX2, -N(T)Y, wherein Y is as defined above, T is selected from hydrogen or X2; and X2 is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms,

When R1 is N(Z)Y or C(Z)Y, at least one of the groups R2, R3, R4 and R5 are selected from the group consisting of –OX2 or -N(T)Y, and the others are independently selected from hydrogen, -OH, -OX2, -N(T)Y, wherein Y is as defined above, T is selected from hydrogen or X2; and X2 is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms,

It is understood that the rules of molecular stoichiometry will be upheld by the default addition of hydrogens atoms as required.

The groups Z and Y may be combined to form a monocyclic or bicyclic ring structure of 4 to 10 atoms. This ring structure may be further substituted with X groups;

The groups R2, R3, R4 and R5 are independently selected from hydrogen, OH, , NHDde, NHDTPM and other vinylogous amines, N(Z)Y, wherein N(Z)Y is as defined above, OX and X is independently selected from

alkyl, alkenyl, alkynyl, heteroalkyl, aminoalkyl, aminoaryl, aryloxy, alkoxy, heteroaryloxy, aminoaryl, aminoheteroaryl, thioalkyl, thioaryl or thioheteroaryl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms which is optionally substituted, branched and/or linear. Typical substituents include but are not limited to OH, NO, NO_2, NH_2, N_3, halogen, CF_3, CHF_2, CH_2F, nitrile, alkoxy, aryloxy, amidine, guanidiniums, carboxylic acid, carboxylic acid ester, carboxylic acid amide, aryl, cycloalkyl, heteroalkyl, heteroaryl, aminoalkyl, aminodialkyl, aminotrialkyl, aminoacyl, carbonyl, substituted or unsubstituted imine, sulfate, sulfonamide, phosphate, phosphoramide, hydrazide, hydroxamate, hydroxamic acid;

With the proviso that when R2 is N(Z)Y, R6 and R7 are hydrogen, and R4 and R5 are OH or together form a benzylidene or substituted benzylidene, then R1 cannot be N(Z)Y.

A preferred embodiment of the first aspect provides for compounds of formula I in which R1 is H and R4 is N(Z)Y;

In a particularly preferred embodiment R1 is H and R4 is N(Z)Y wherein Z is hydrogen;

A further embodiment of the first aspect provides for compounds of formula I in which R1 and R4 are independently N(Z)Y;

Another embodiment provides for compounds of formula I in which R1 is H and both R2 and R4 are N(Z)Y;

In a preferred embodiment provides for compounds of formula I in which the ring is of the gluco, galacto or allo configuration;

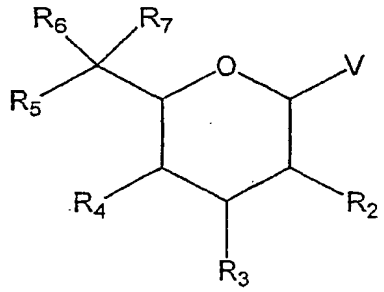
A further embodiment provides for compounds of formula I in which R1 is N(Z)Y and R2 is N(Z)Y;

A further embodiment provides for compounds of formula I in which R1 is P(Z)Y and R2 is N(Z)Y, wherein P is carbon and Y is hydrogen.

A further embodiment provides for compounds of formula I in which R1 is P(Z)Y and R4 is N(Z)Y, wherein P is carbon and Y is hydrogen.

A further embodiment provides for compounds of formula I in which R1 is N(Z)Y and R5 is N(Z)Y and the ring is of the furan form.

In a second aspect, the invention provides for a method of synthesis of compounds of formula I in which R1 is hydrogen, comprising the step of reducing a synthetic intermediate of formula II, in which the substituent V is either bromine or chlorine, R6 and R7 are as defined in the first aspect, R5, R4, R3, and R2 are independently selected from OH, O-acyl, N_3, NHDde, NHDTPM, NHZ, NHBOC, phthalimide, O-protecting group or when R6 and R7 together for a carbonyl oxygen, R5 may additionally be optionally substituted O-alkyl, O-arylalkyl or O-aryl. Where the protecting groups may be chosen from any suitable oxygen protecting groups known in the art, including acetals and ketals which protect two adjacent oxygens.



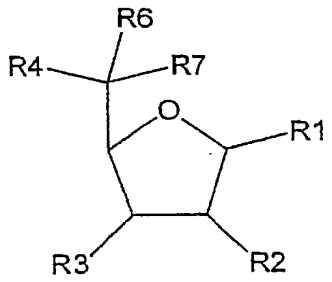
formula II

In a third aspect, the invention provides for a method of synthesis of compounds of formula I in which R1 is N(Z)Y comprising the step of reacting a compound of formula II with and azide nucleophile, in which the substituents for formula II are as described in the second aspect.

aspect, R4, R3, and R2 are independently selected from OH, O-acyl, N_3, NHDde, NHDTPM, NHZ, NHBOC, phthalimide, O-protecting group or when R6 and R7 together for a carbonyl oxygen, R4 may additionally be optionally substituted O-alkyl, O-arylalkyl or O-aryl. Where the protecting groups may be chosen from any suitable oxygen protecting groups known in the art, including acetals and ketals which protect two adjacent oxygens.

In a sixth aspect, the invention provides for a method of synthesis of compounds of formula I in which R1 is H, comprising the step of reducing a compound of formula IV in which the substituents for formula II are as described in the fifth aspect.

In a seventh aspect, the invention provides for a method of combinatorial synthesis of compounds of formula I comprising the step of immobilizing a compound of formula V onto an support. Said support may be soluble or insoluble. Non-limiting examples of insoluble supports include derivatised polystyrene, tentagel, wang resin, MBHA resin, aminomethylpolystyrene, rink amide resin etc., Non-limiting examples of soluble supports include DOX-mpeg, polyethylene glycol etc.



formula V

Wherein R1 is as defined in the first aspect, R2, R3, R4, R6 and R7 are as defined in the fifth aspect, and the linkage between the compound of formula V and the support is through any of positions R2, R3, or R4.

General Solution and Solid Phase Methods For Examples 1-21

General Method 1: Formation of a Glycosyl Bromide

To a solution of the anomeric-acetate compound (100 mmol) in dichloromethane (250 mL) at 0°C, was added a solution of 33% HBr in acetic acid (100mL). The solution was then stirred for 2 h at room temperature. At this time chloroform was added to the suspension and the resulting solution poured onto ice/water. The chloroform layer was then collected and washed with cold water, saturated sodium hydrogen carbonate, brine, dried ($MgSO_4$), and the solvent removed to leave a foam. This foam was trituated with ether (50 mL) for 30 min and the resulting solid filtered to give the glycosyl bromide as a white solid. Yield typically greater than 95%.

General Method 2: Reduction at the Anomeric Centre to Form a Glycitol

To a suspension of glycosyl bromide (100 mmol) in dry toluene 200 mL was added tributyltin hydride (110 mmol) and the whole refluxed under nitrogen for 3 h. The suspension was concentrated to dryness and the residue re-dissolved in a 2:1 dichloromethane/chloroform (250 mL) mixture. To the residue was then added potassium fluoride (20 g) in water (100 mL), and the heterogeneous solution stirred vigorously for 45 min. The resulting suspension was filtered through a pad of celite and washed several times with dichloromethane. The combined filtrates were then washed with water, brine, dried ($MgSO_4$), and solvent removed in vacuo to leave a solid in typically quantitative yield.

General Method 3: Solution Phase Zemplen

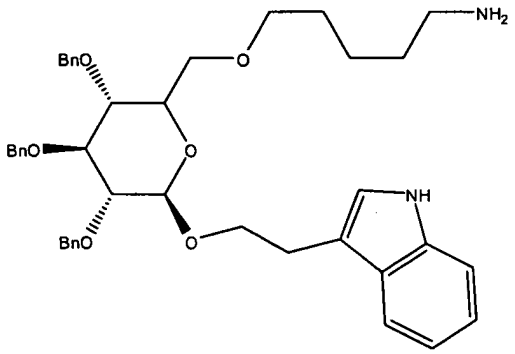
To a suspension of the acetylated compound (100 mmol) in dry methanol (125 mL) at 0°C was added a solution of sodium methoxide (0.33 mmol) in dry methanol (125 mL) and the mixture was stirred under nitrogen for 2 h. Amberlite IR 120 H^+ was added until pH 5 was reached, the solution was filtered and the resin washed several times with a 2:1

ATTACHMENT I

Compounds recited in Hirschmann 6,197,963B1

EXAMPLE 1

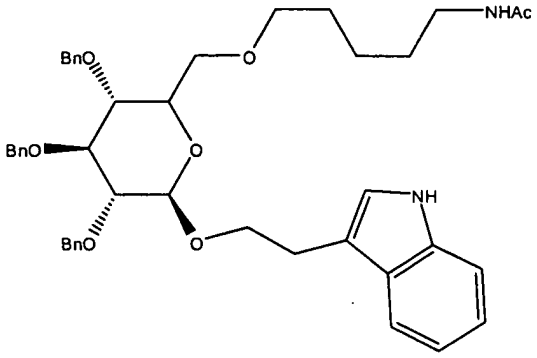
Preparation of Analog Having Structure (1), 2-(1H-Indol-3yl)ethyl-6-O-(5-aminopentyl)-2,3,4-tri-O-benzyl-β-D-glucopyranoside



Same as example 22

EXAMPLE 2

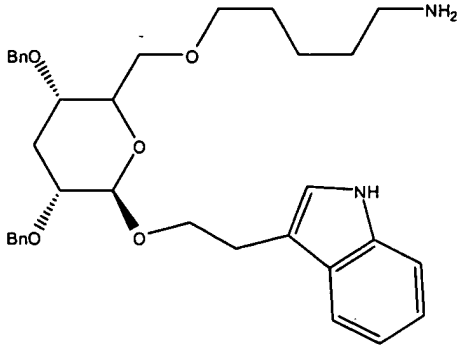
Preparation of Analog Having Structure (7), 2-(1-Phenylsulfonyl-indol-3yl)ethyl-6-O-(5-acetamidopentyl)-2,3,4-tri-O-benzyl-β-D-glucopyranoside



EXAMPLE 3

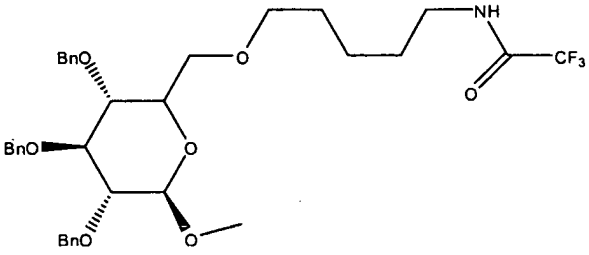
Preparation of Analog Having Structure (2), 2-(1H-indol-3-yl)ethyl-6-O-(5-aminopentyl)-2,4-di-O-deoxy-β-D-glucopyranoside

Compound name contains an error and should be 2-(1H-indol-3-yl)ethyl-6-O-(5-aminopentyl)-2,4-di-O-benzyl-3-deoxy-b-D-glucopyranoside as evidenced by the method of preparation.



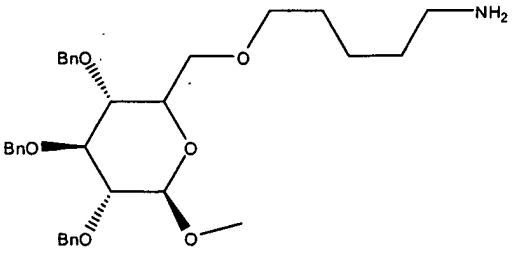
EXAMPLE 4

Preparation of Analog Having Structure (13), Methyl 2,3,4-tri-O-benzyl-6-O-(N-trifluoroacetyl-5-aminopentyl)-β-D-glucopyranoside



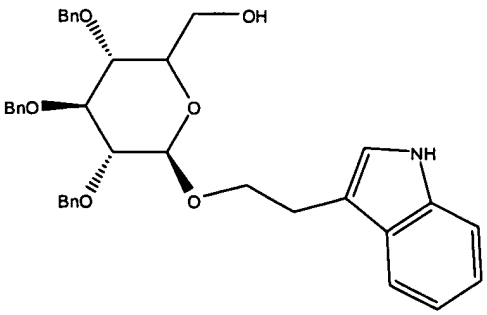
EXAMPLE 5

Preparation of Analog Having Structure (8), Methyl 6-O-(5-aminopentyl)-2,3,4-tri-O-benzyl-β-D-glucopyranoside



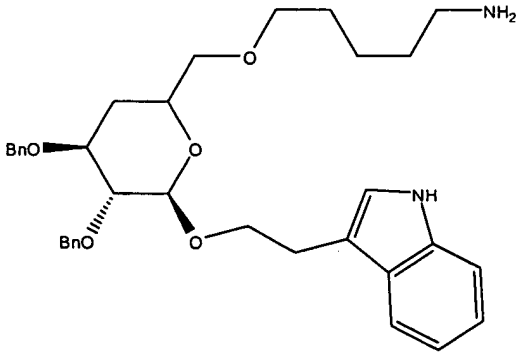
EXAMPLE 6

Preparation of Analog Having Structure (12), 2-(1H-Indol-3yl)ethyl-2,3,4-tri-O-benzyl-β-glucopyranoside



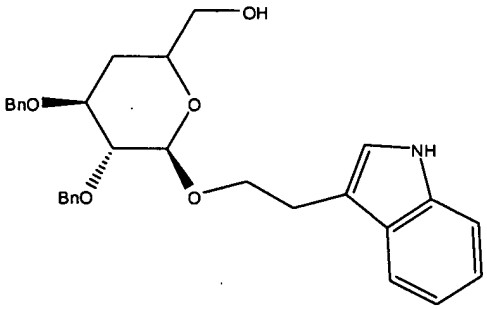
EXAMPLE 7

Preparation of Analog Having Structure (10), 2-(1H-Indol-3-yl)ethyl-6-O-aminopentyl)-2,3-di-O-benzyl-4-deoxy-β-D-glucopyranoside



EXAMPLE 8

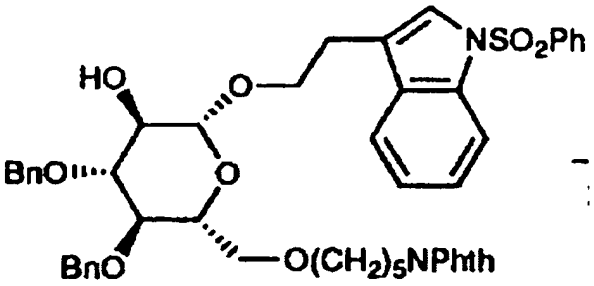
Preparation of Analog Having Structure (11), 2-Indol-3-yl-ethyl-2,3,-di-O-benzyl-4-deoxy-β-D-glucopyranoside



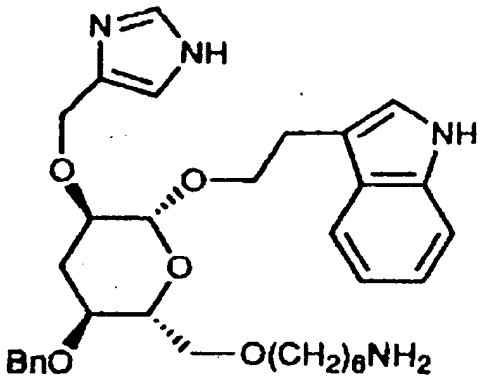
EXAMPLE 9

Preparation of Imidazol Compounds

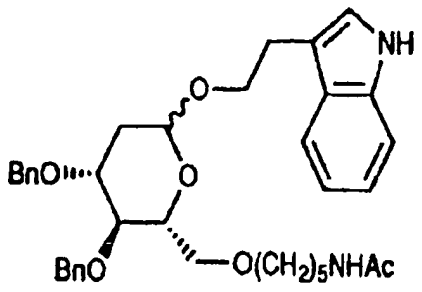
Compounds in this example which are repeated in other examples are not shown.



I-23

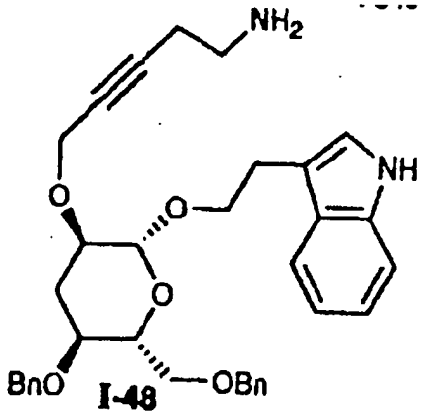


I-16

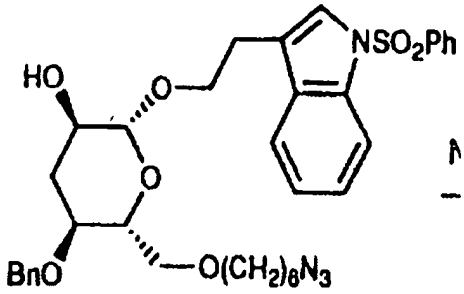


I-29α 14%

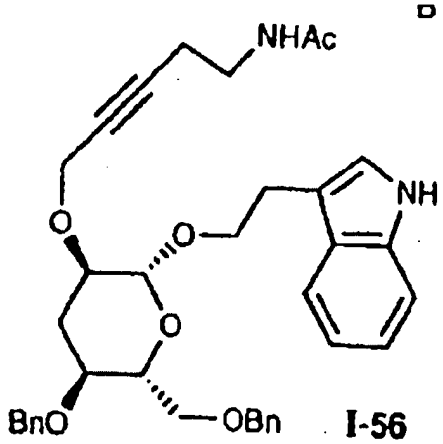
I-29β 6%



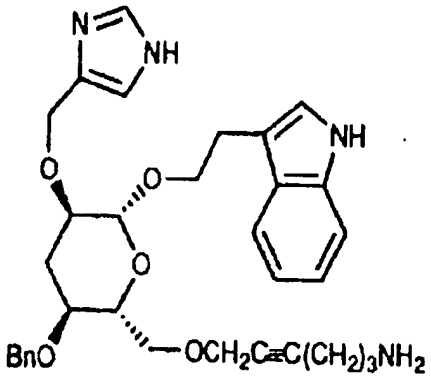
I-48



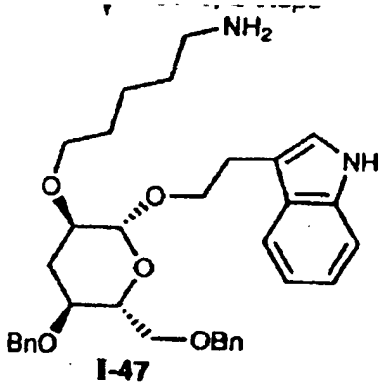
I-36



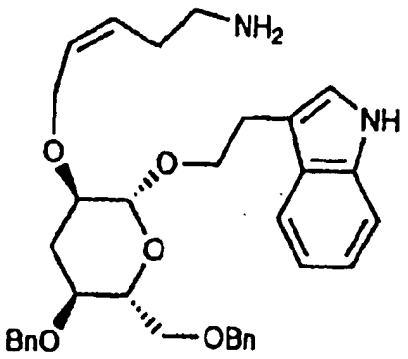
I-56



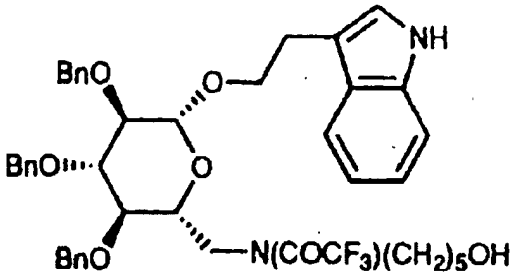
I-42



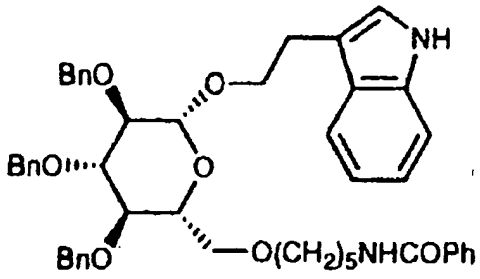
I-47


NH2
NH
O
O
O
BnO
OBn

I-49

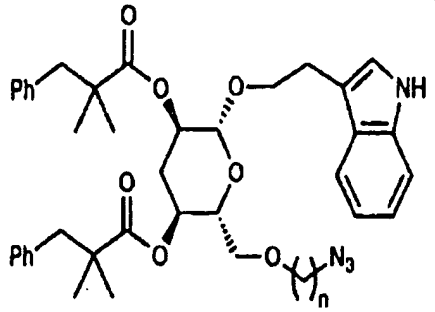

NH
BnO
O
BnO
O
BnO
N(COCF3)(CH2)5OH

I-58

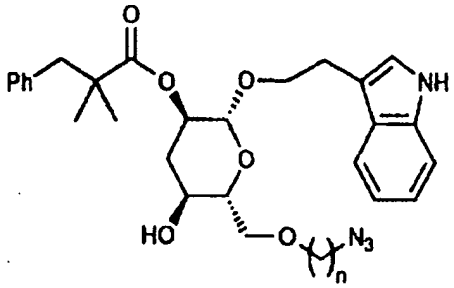

NH
BnO
O
BnO
O
BnO
O(CH2)5NHCOPh

EXAMPLE 10

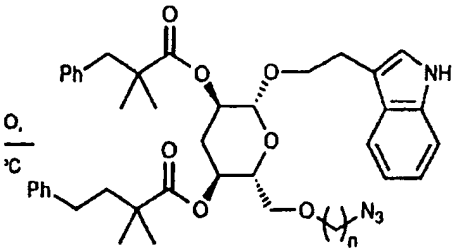
Preparation of Ester Compounds



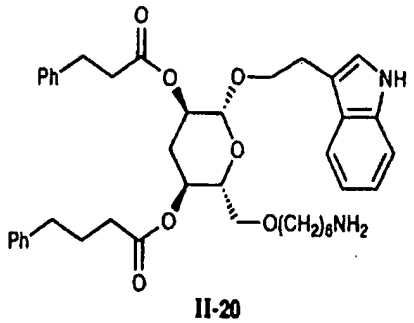
II-17 **a**; n = 6 16 h:
b; n = 5 40 h:



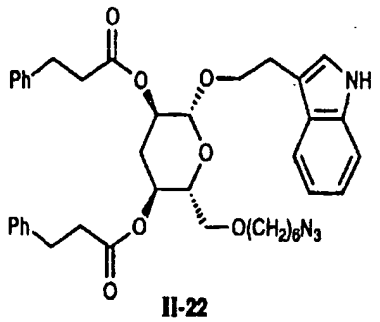
0% 14a 30% **II-18** **a**; n = 6
61% 14a 31% **b**; n = 5



II-19 **a**; n = 6
b; n = 5



II-20



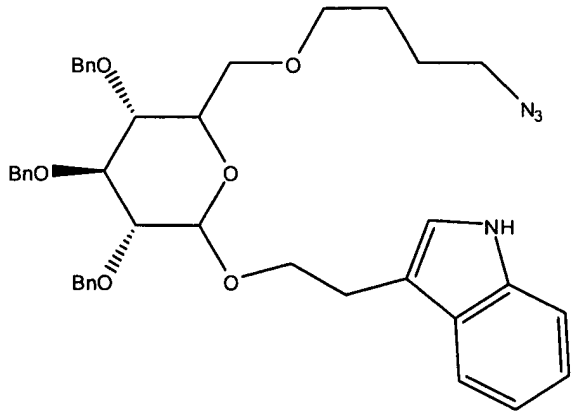
II-22

EXAMPLE 11

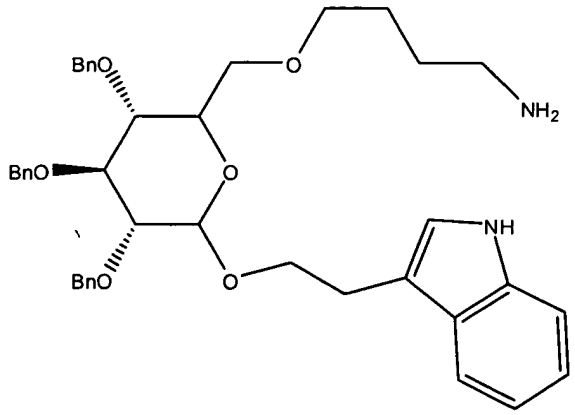
Preparation of Other Compounds

Non-carbohydrate compounds have been left out of this summary.

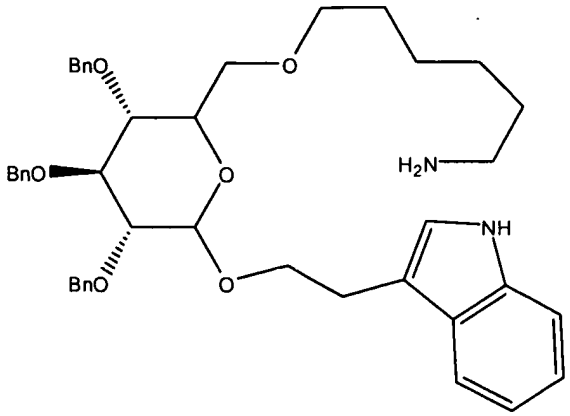
A. III-12 non-carbohydrate
B. III-13 – same as example 1c
C. III-14 – same as example 1d
D. III-15 – same as example 1e
E. III-16 – same as example 1f
F. III-17 – same as example 1 g
G. III-19a- same as example 22
H. III-4a - same as example 24
I. III-19b



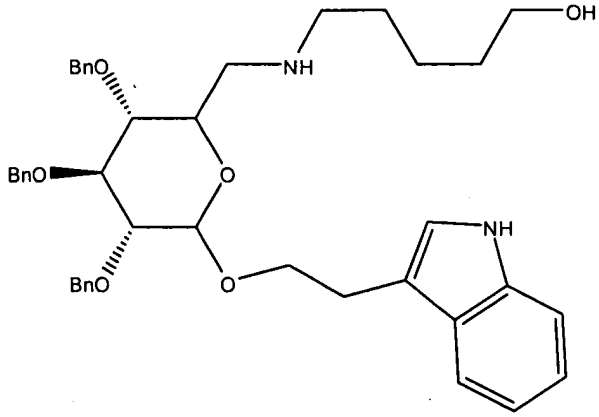
J. III-4b



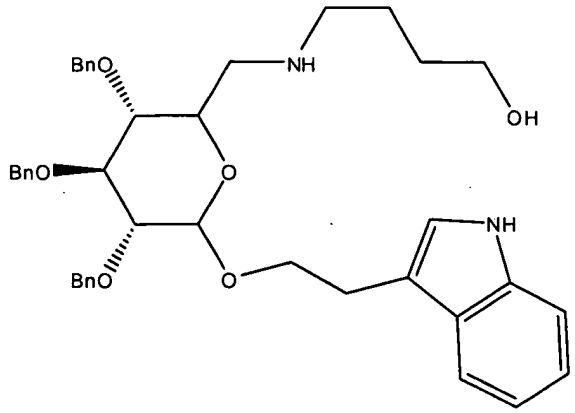
K. III-19c sulfonamide of L below
L. III-4c



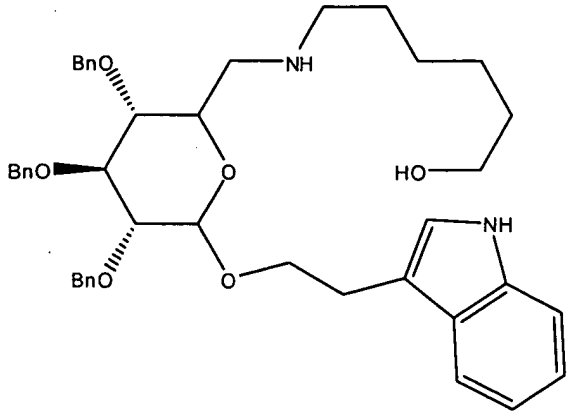
M. III-18a non-carbohydrate
N. III-4c (expect this is a typo) – same as



O. III-18b non-carbohydrate
P. III-4f

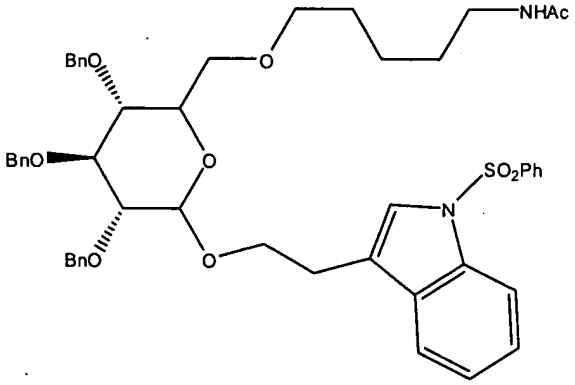


Q. III-4g

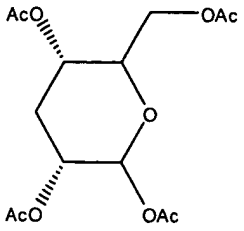


R. III-20 non-carbohydrate

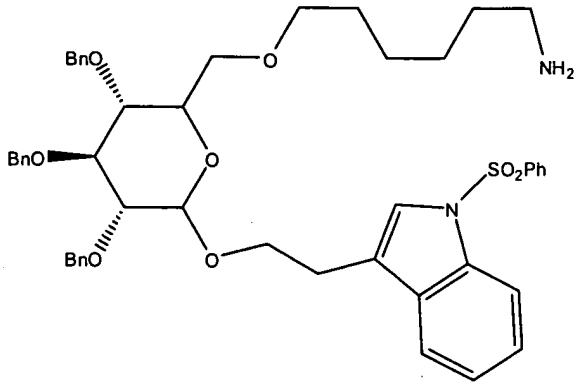
S. III-4d



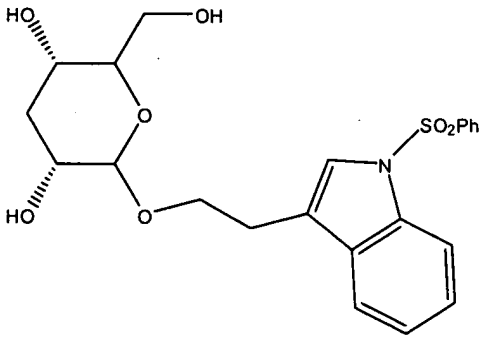
T. III-23



U. III-24



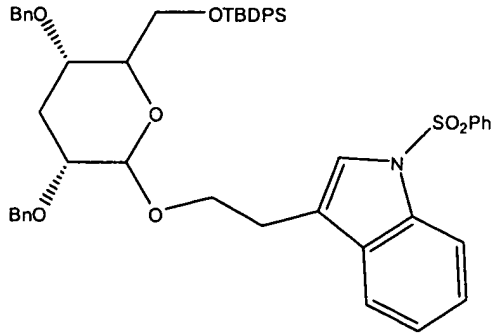
V. III-25



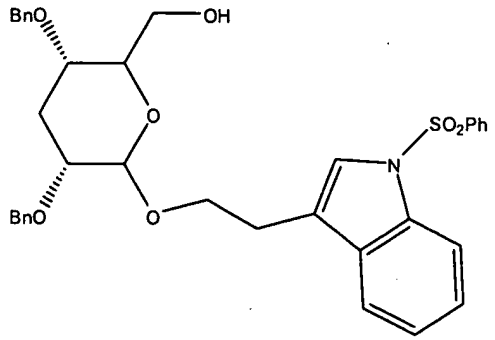
W. III-26

6-tertbutyldiphenylsilyl III-25

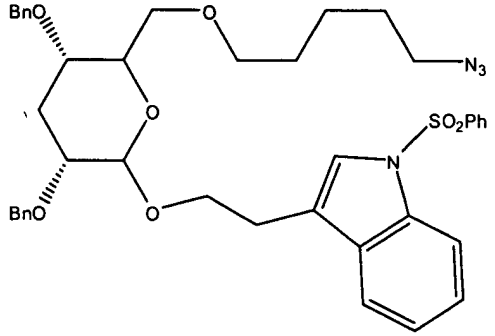
X. III-27



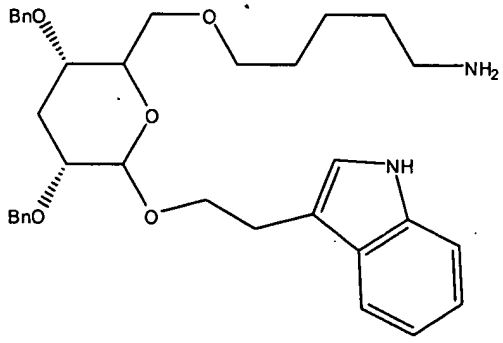
Y. III-28



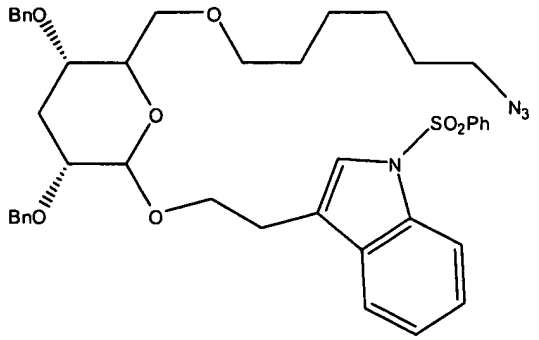
Z. III-29a



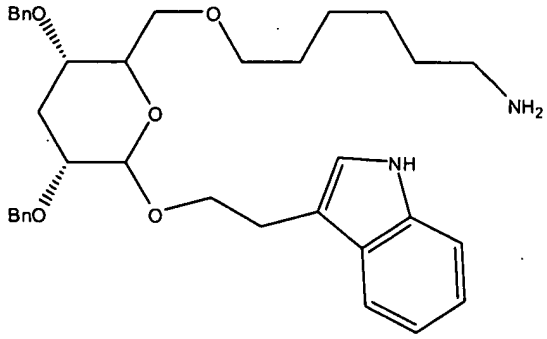
AA. III-5a



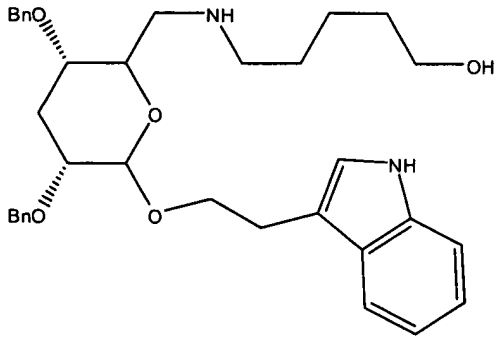
AB. III-29b



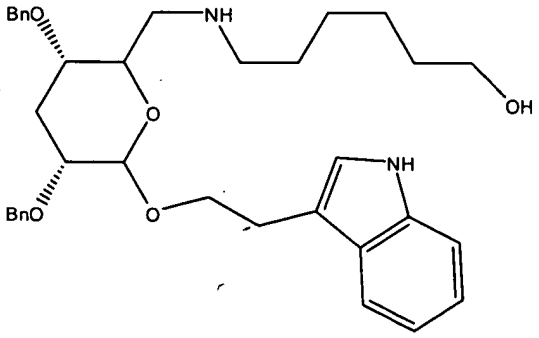
AC. III-5b



AD. III-5c

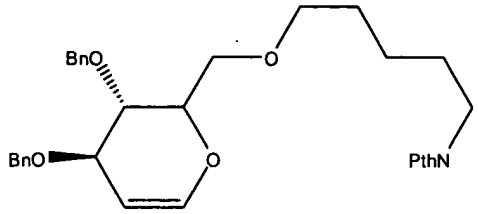


AE. III-5d

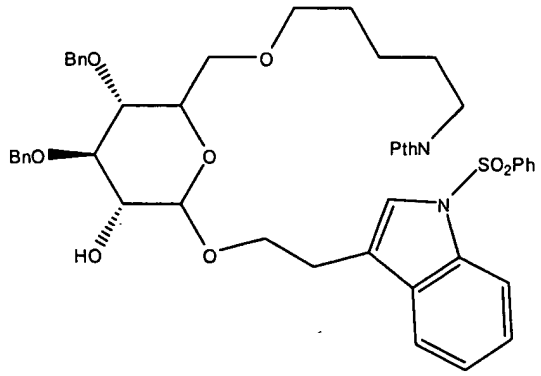


AF. III-33 non-carbohydrate

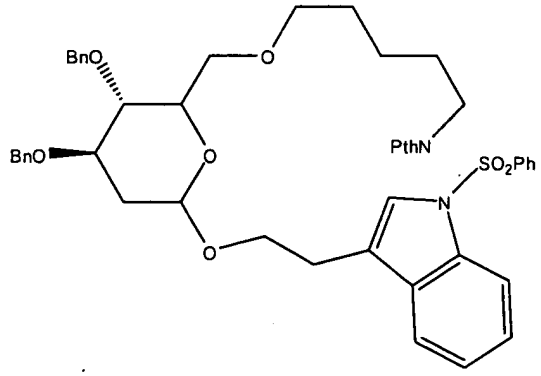
AG. III-34



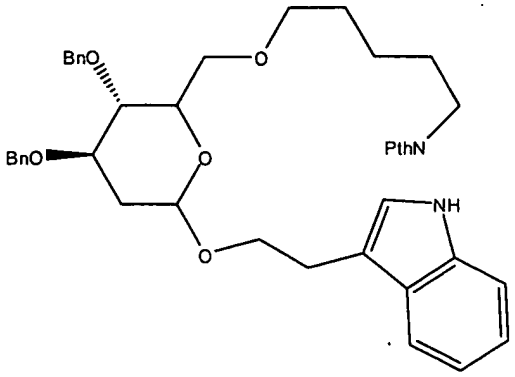
AH. III-35



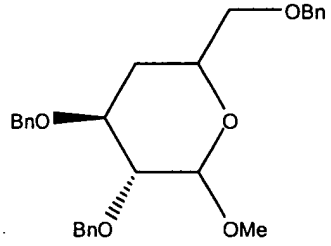
AI. III-36
Incorrectly named in specification



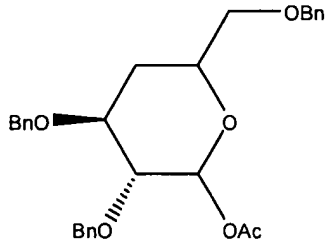
AJ. III-6



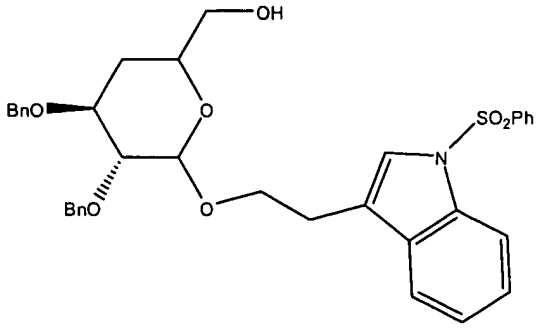
AK. III-38



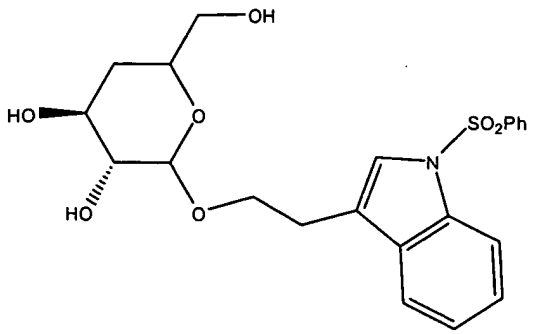
AL. III-39



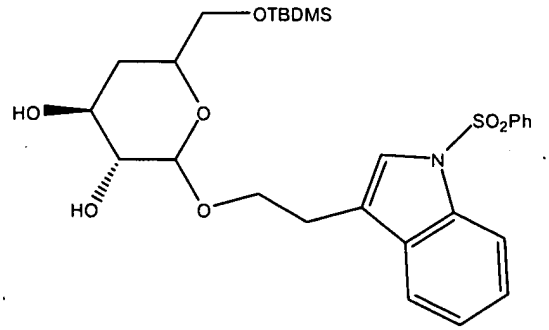
AM. III-40



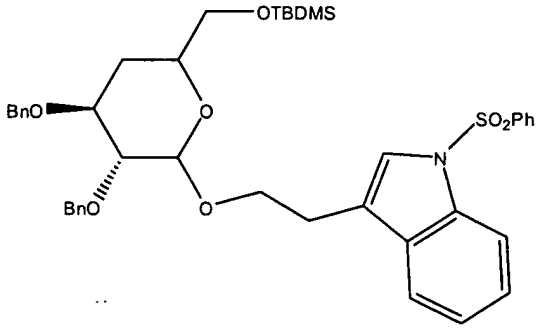
AN. III-41



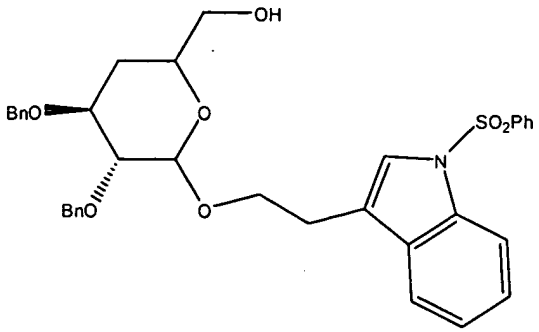
AO. III-42



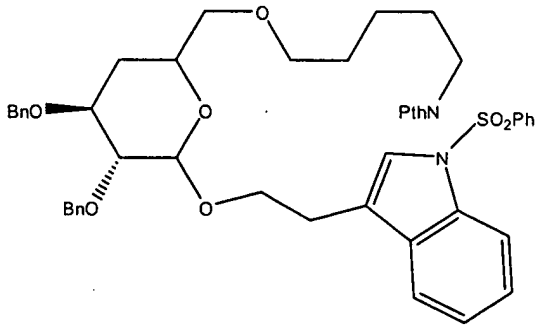
AP. III-43



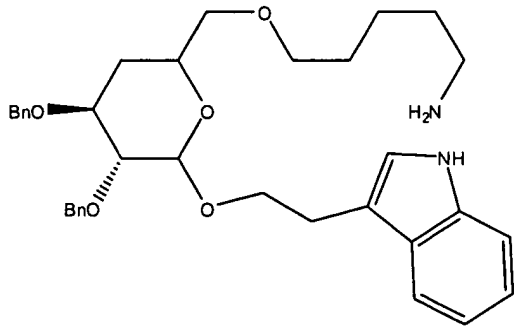
AQ. III-44



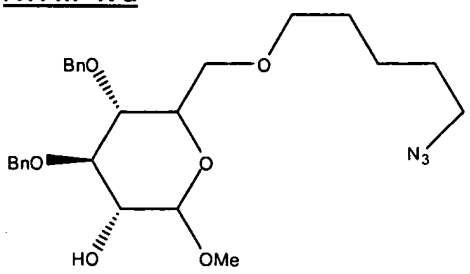
AR. III-45



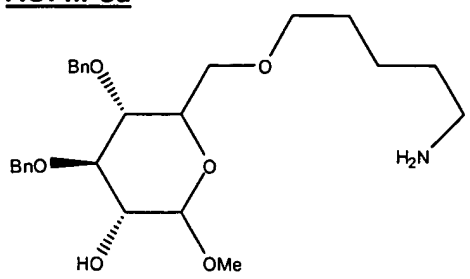
AS. III-7



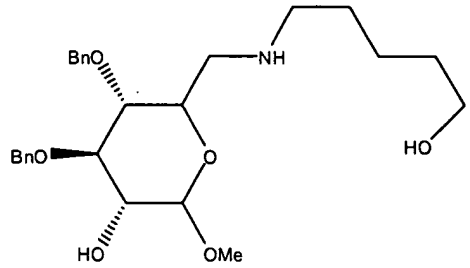
AT. III-47a



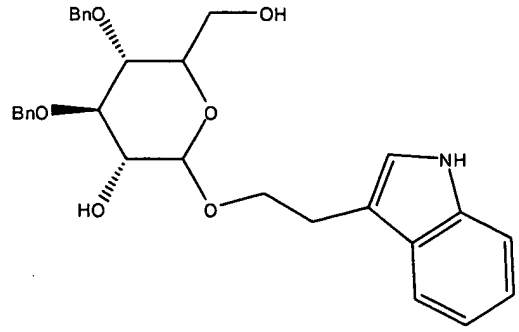
AU. III-8a



AV. III-8b

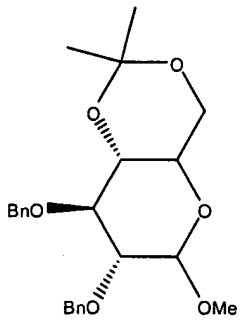


AW. III-9

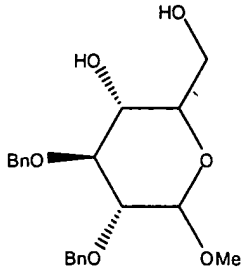


A

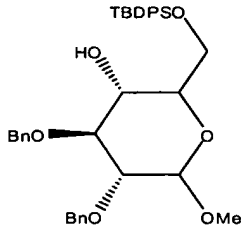
X. III-50



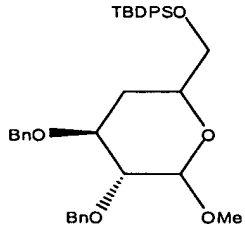
AY. III-51



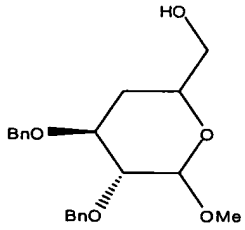
BA. III-52



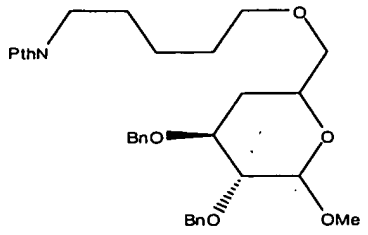
BB. III-53



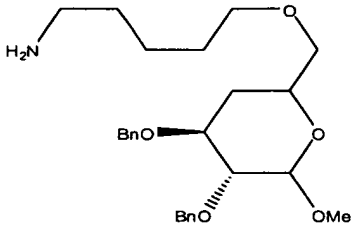
BC. III-54



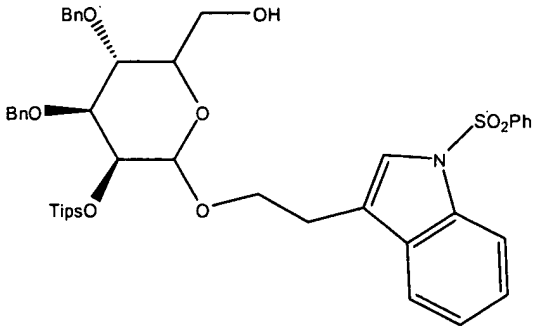
BD. III-55



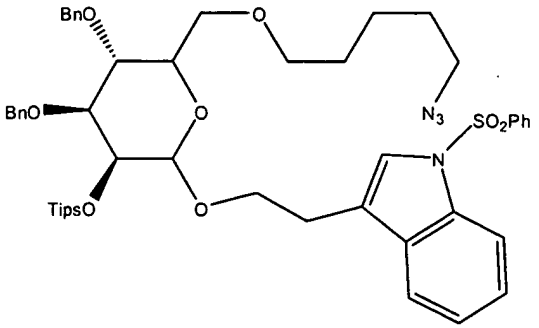
E. III-10



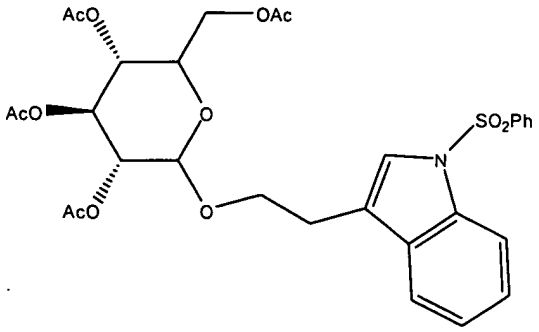
Example 15 - compound IV-1



Example 16 compound IV-2

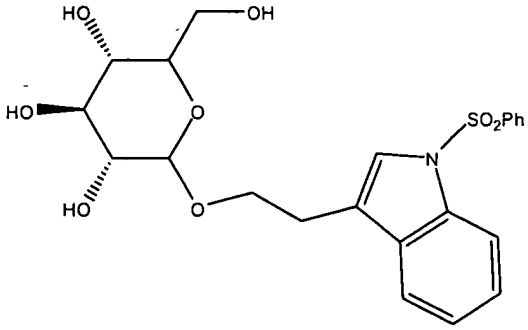


Example 17 compound IV-3

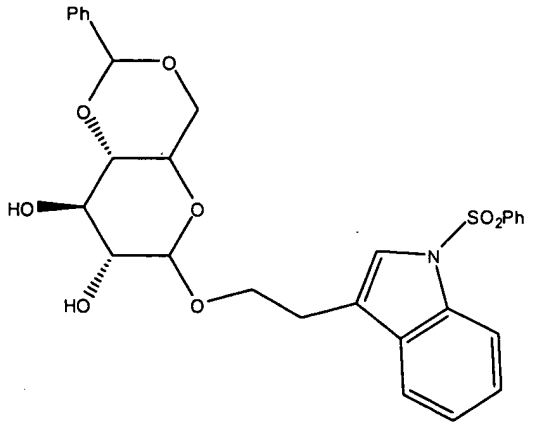


B

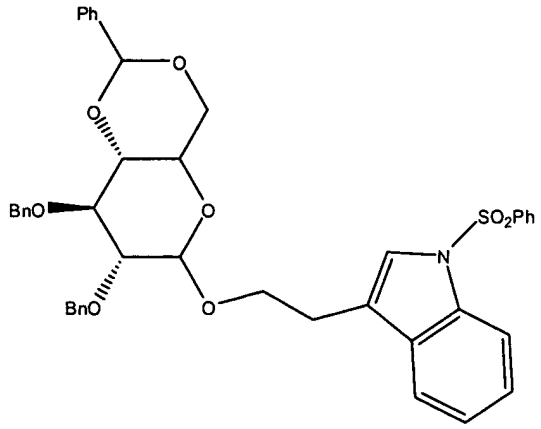
Example 18 compound IV-5



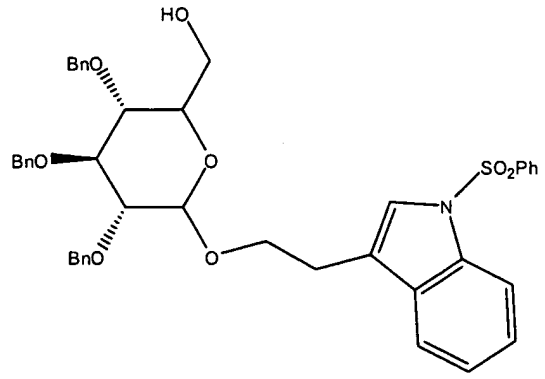
Example 19 compound IV-6



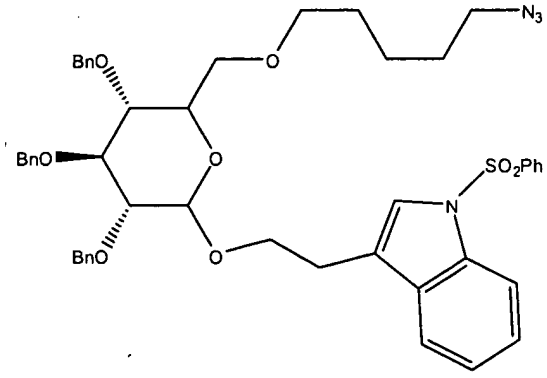
Example 20 compound IV-7



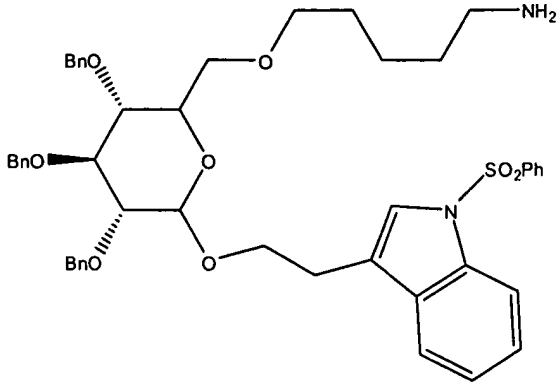
Example 21 compound IV-8



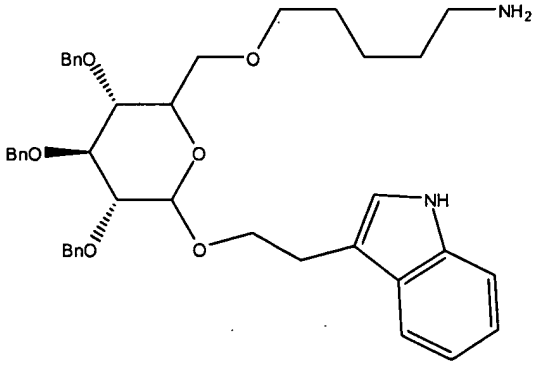
Example 22 compound IV-9



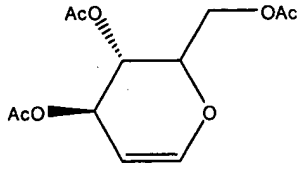
Example 23 compound IV-10



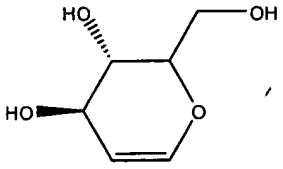
Example 24 compound IV-11



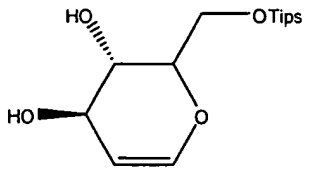
Example 25 compound IV-13



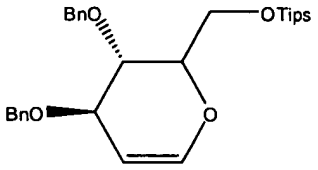
Example 26 compound IV-14



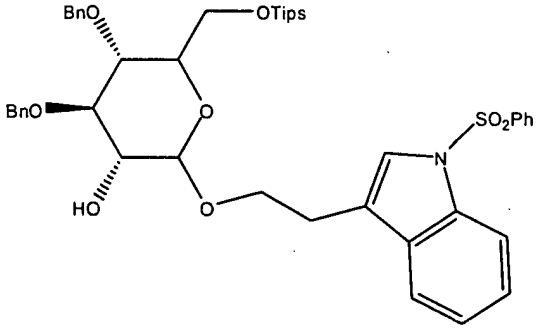
Example 27 compound IV-15



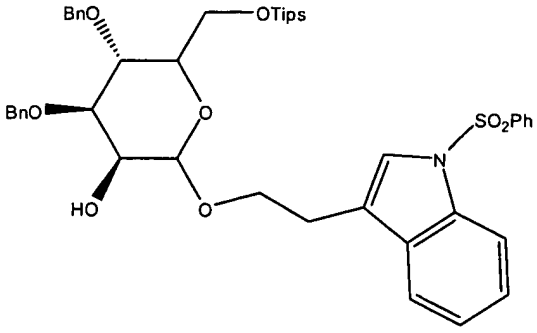
Example 28 compound IV-16



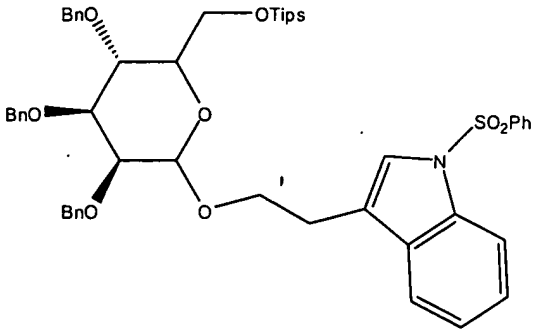
Example 29 compound IV-17



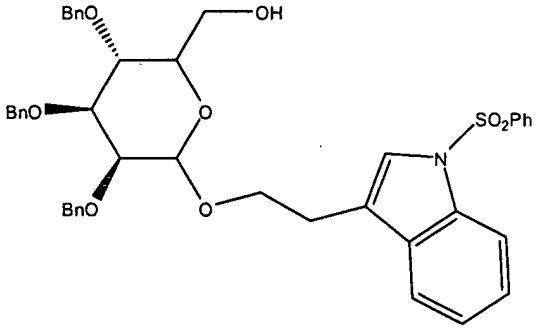
Example 30 compound IV-18



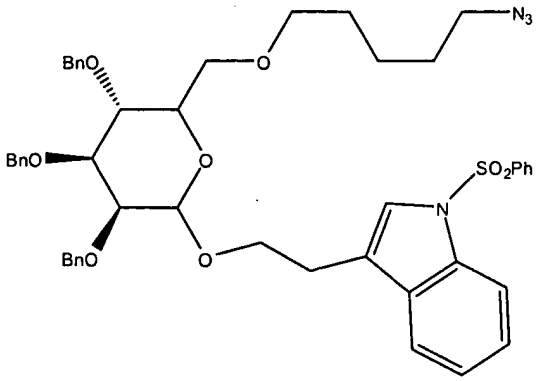
Example 31 compound IV-19



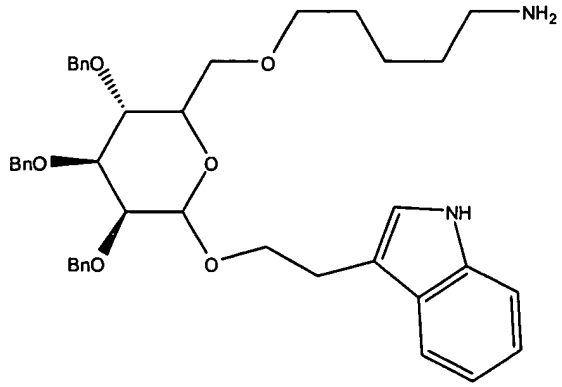
Example 32 compound IV-20



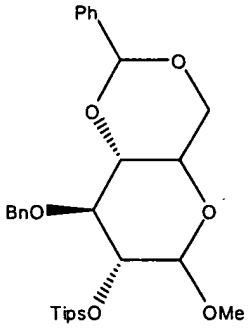
Example 33 compound IV-21



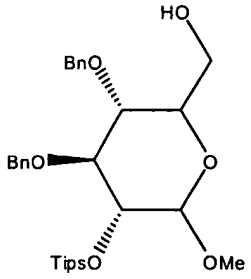
Example 34 compound IV-22



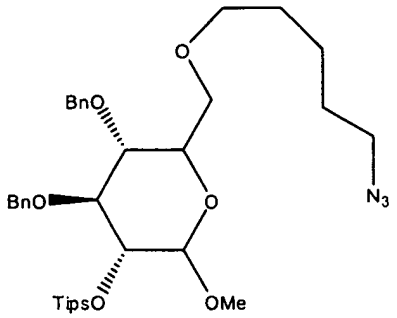
Example 35 compound IV-24



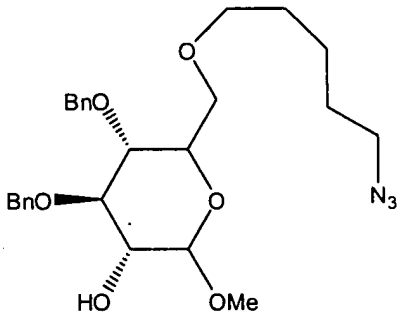
Example 36 compound IV-25



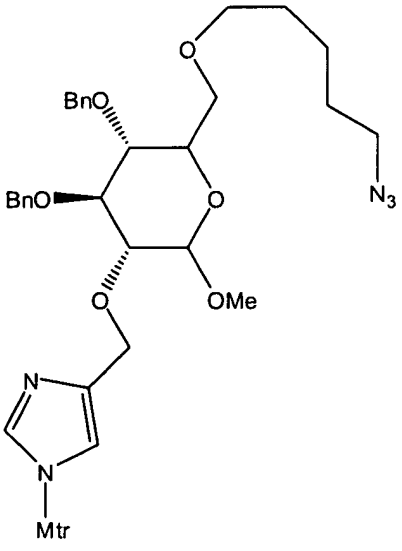
Example 37 compound IV-26



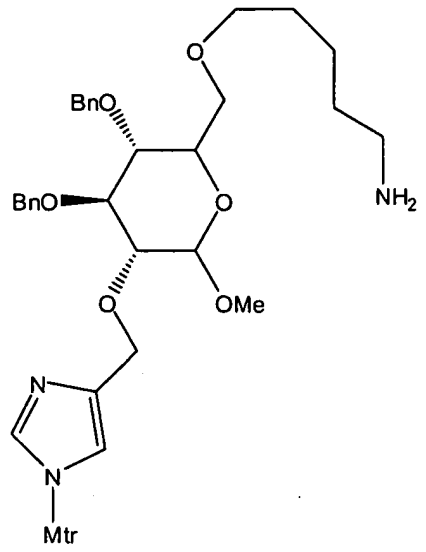
Example 38 compound IV-27



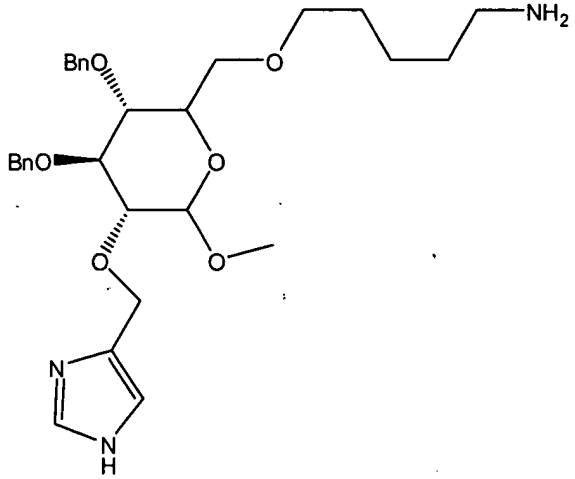
Example 39 compound IV-28



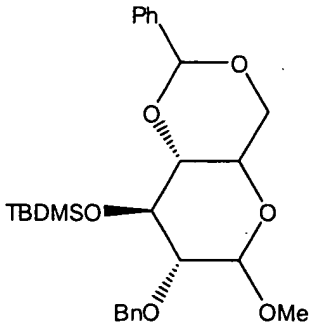
Example 40 compound IV-29



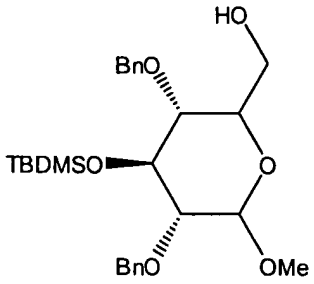
Example 41 compound IV-30



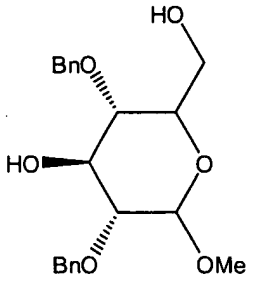
Example 42 compound IV-32



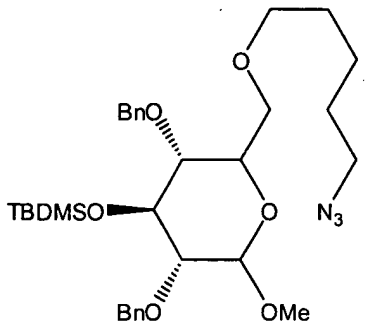
Example 43 compound IV-34



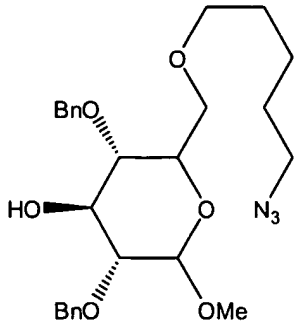
Example 44 compound IV-33



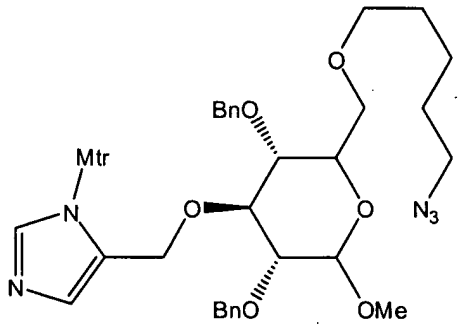
Example 45 compound IV-35



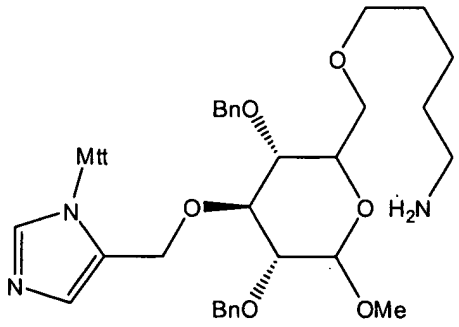
Example 46 compound IV-36



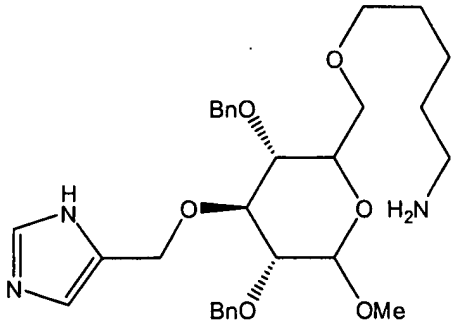
Example 47 compound IV-37



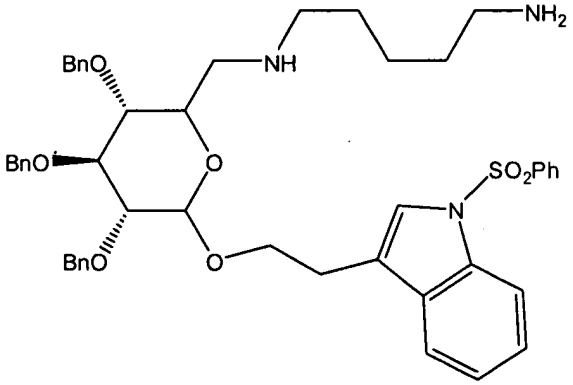
Example 48 compound IV-38



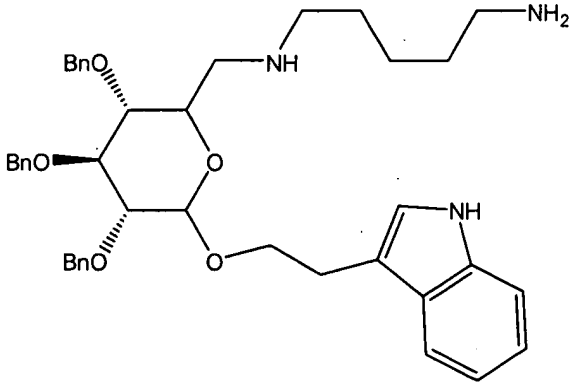
Example 49 compound IV-39



Example 50 compound IV-41



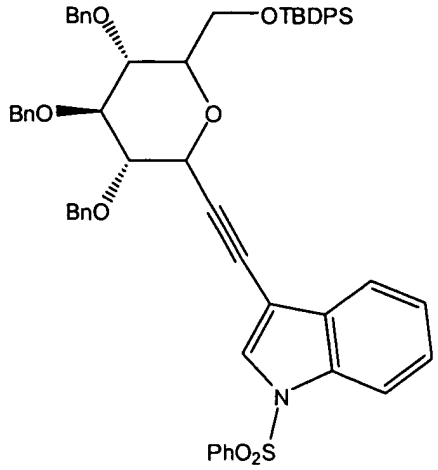
Example 51 compound IV-42



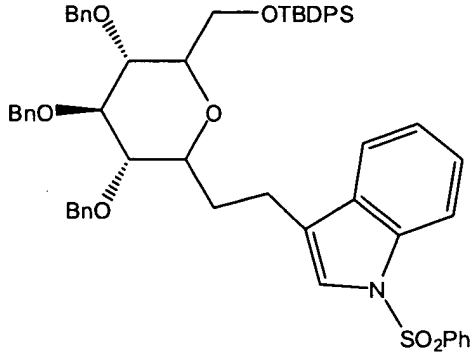
Example 52 compound IV-43 & IV-44

Non-carbohydrate compounds

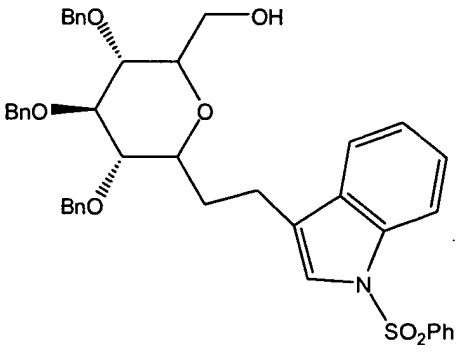
Example 53 compound IV-46



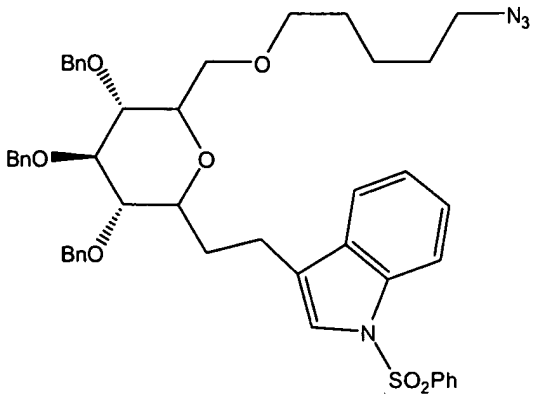
Example 54 compound IV-47



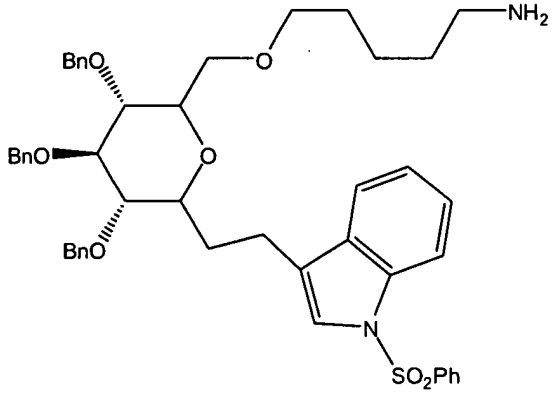
Example 55 compound IV-48



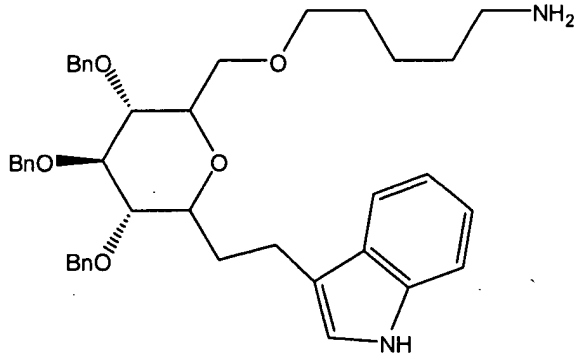
Example 56 compound IV-49



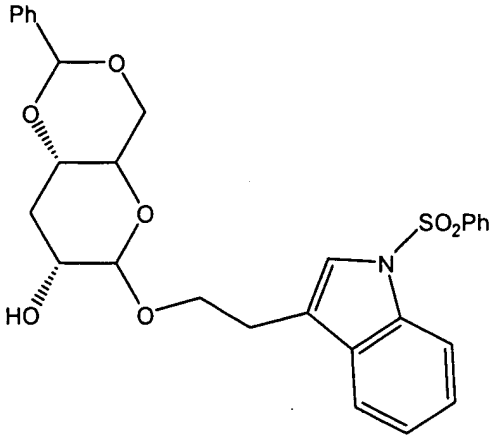
Example 57 compound IV-51



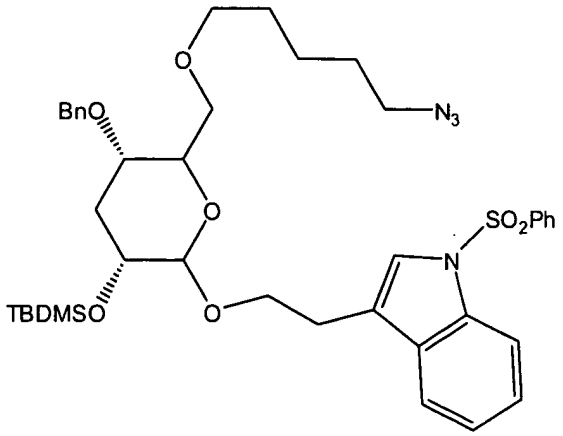
Example 58 compound IV-50



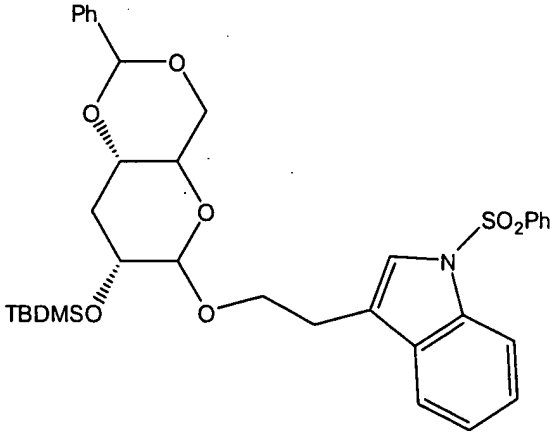
Example 59 compound IV-53



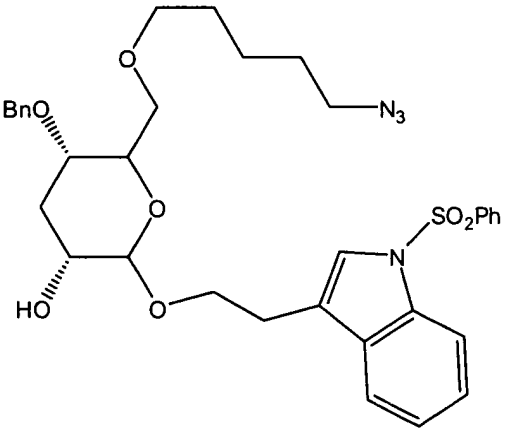
Example 62 compound IV-56



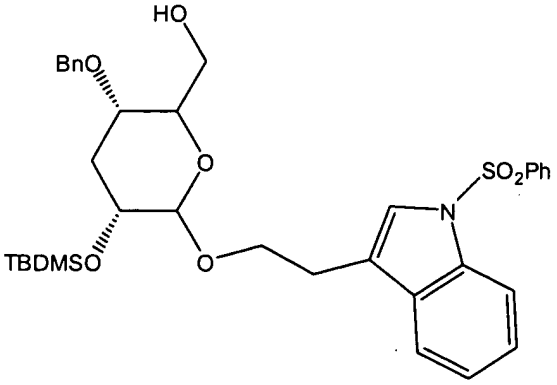
Example 60 compound IV-54



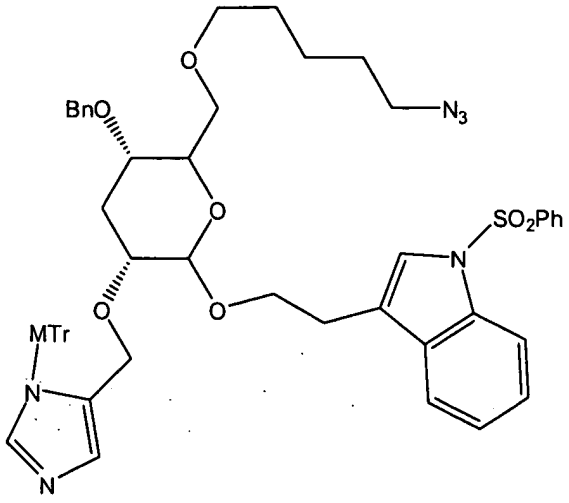
Example 63 compound IV-57



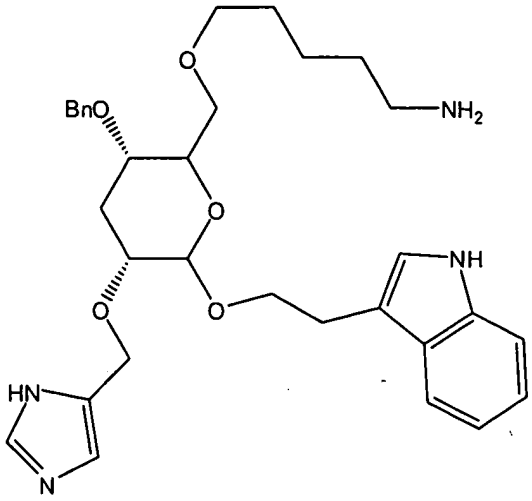
Example 61 compound IV-55



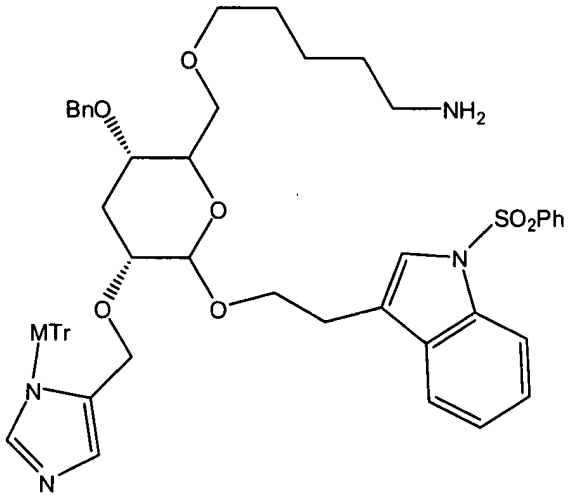
Example 64 compound IV-58



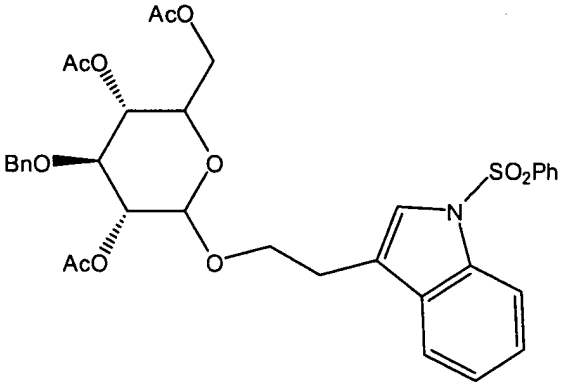
Example 66 compound IV-60



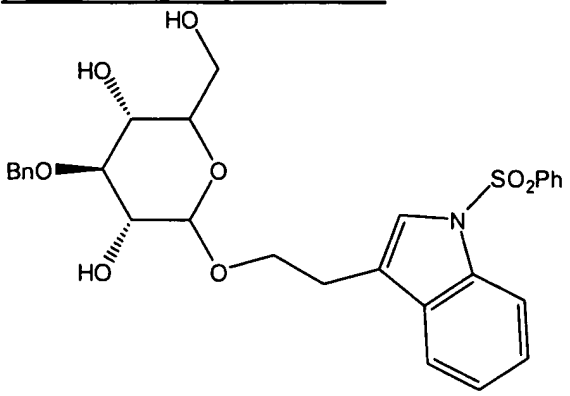
Example 65 compound IV-59



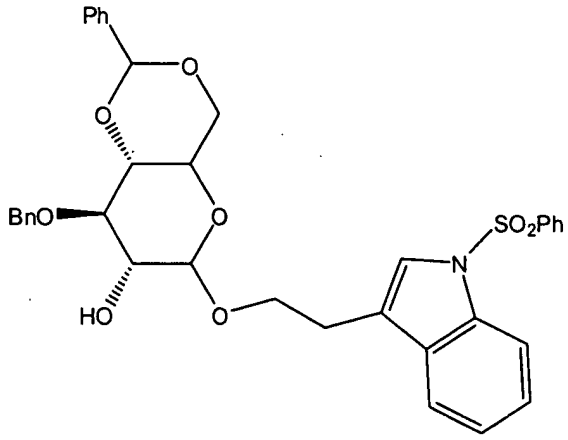
Example 67 compound IV-62



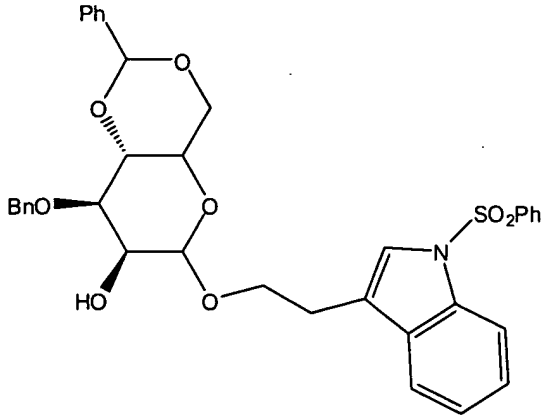
Example 68 compound IV-63



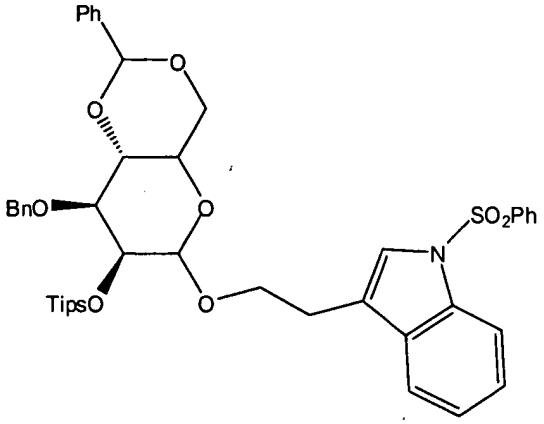
Example 69 compound IV-64



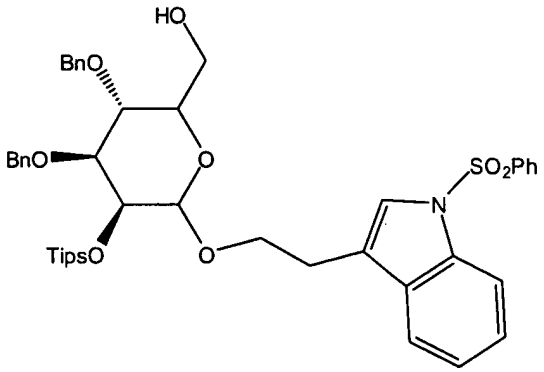
Example 70 compound IV-65



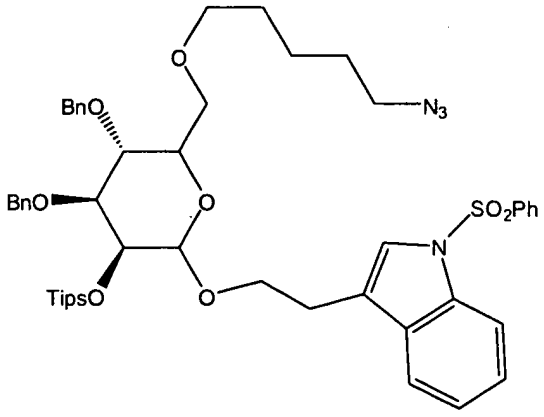
Example 71 compound IV-66



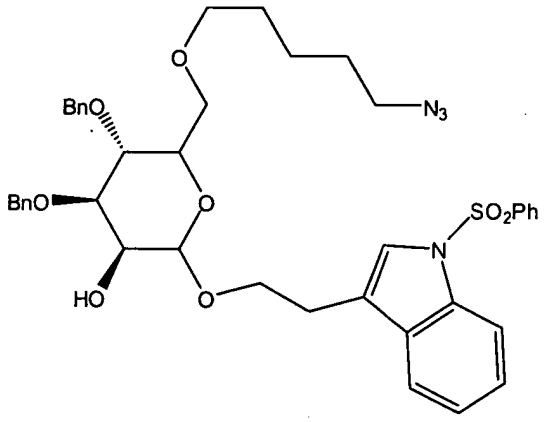
Example 72 compound IV-67



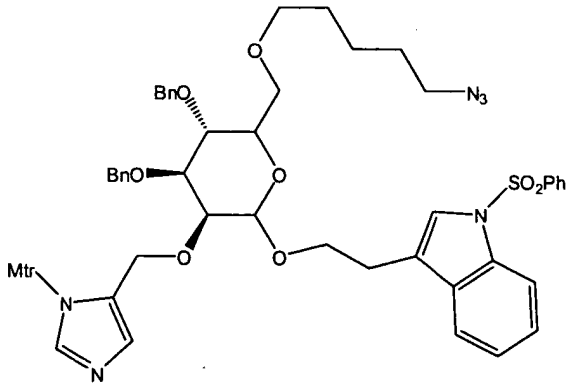
Example 73 compound IV-68



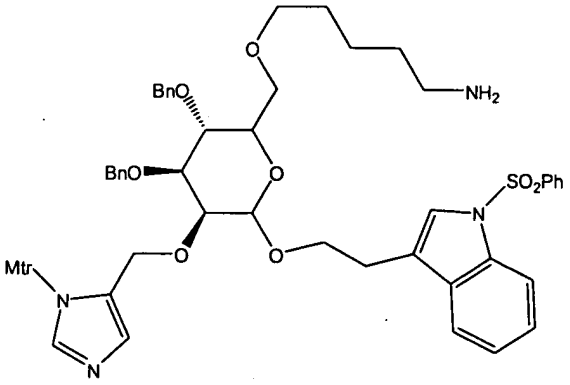
Example 74 compound IV-69



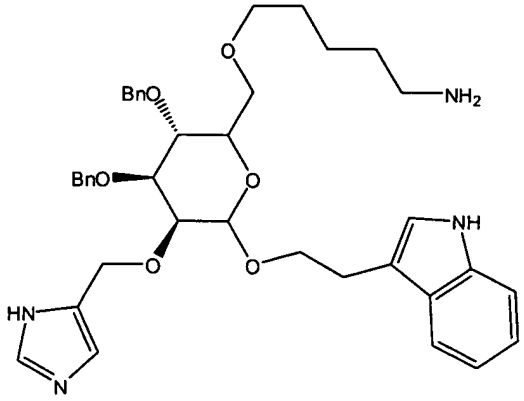
Example 75 compound IV-70



Example 76 compound IV-71



Example 77 compound IV-72



Example 78 compound IV-74

D Isomer of example 67

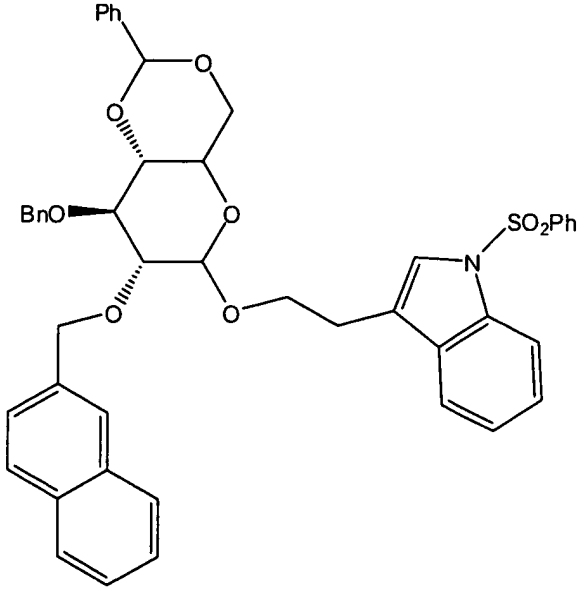
Example 79 compound IV-75

D Isomer of example 68

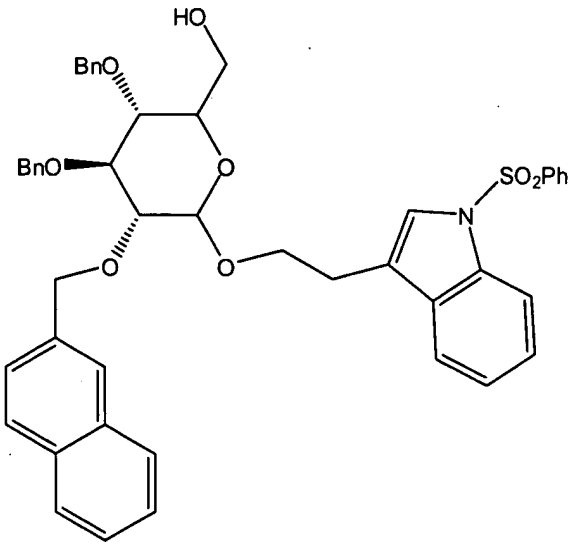
Example 80 compound IV-76

D Isomer of example 69

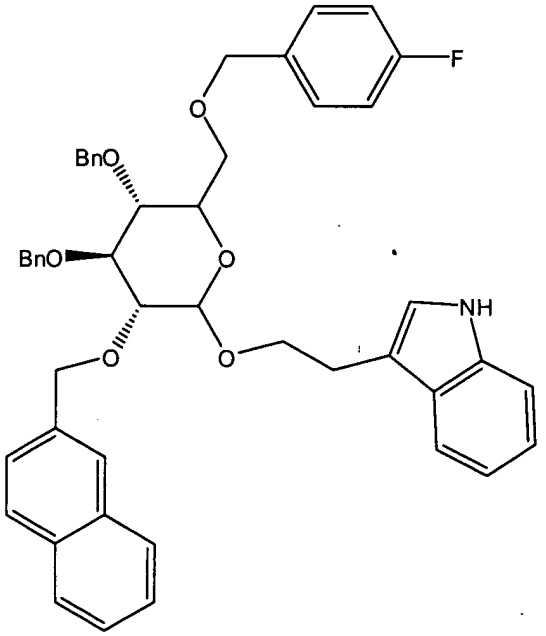
Example 81 compound IV-77



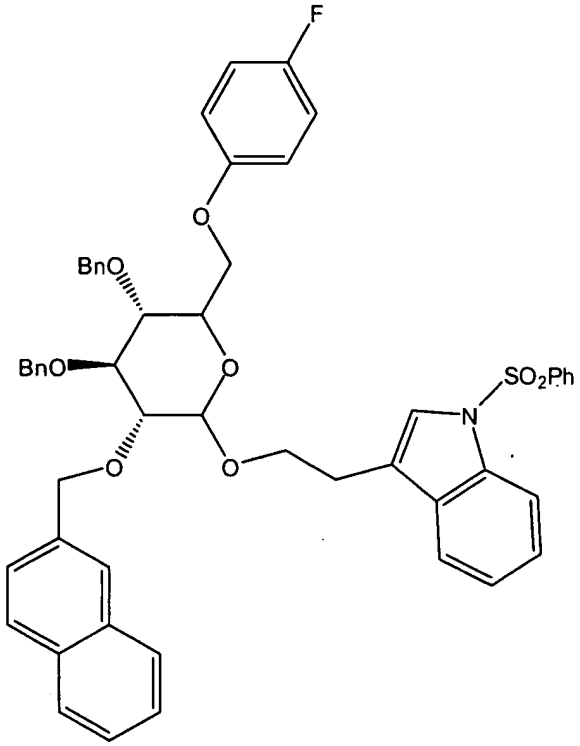
Example 82 compound IV-78



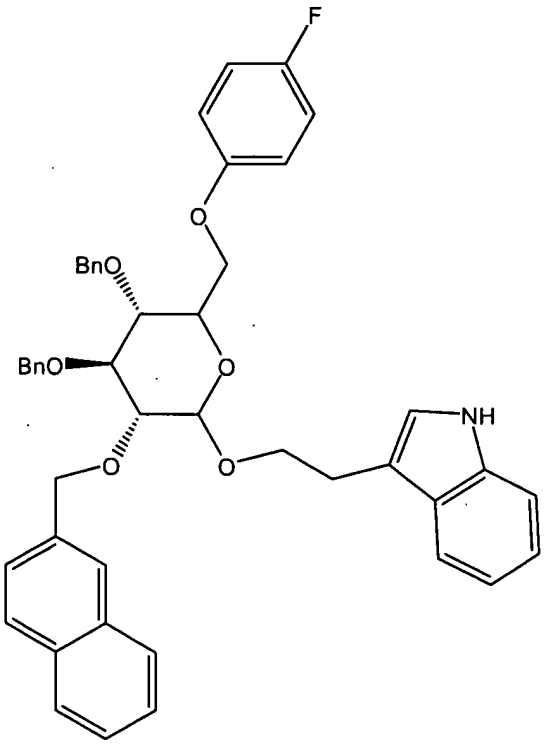
Example 83 compound IV-79



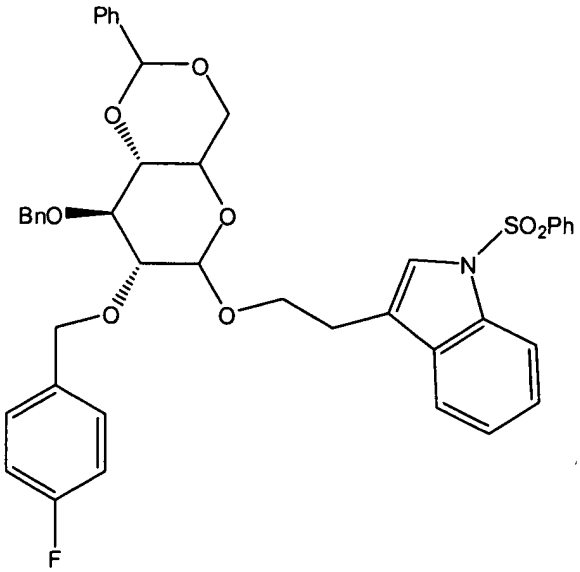
Example 84 compound IV-80



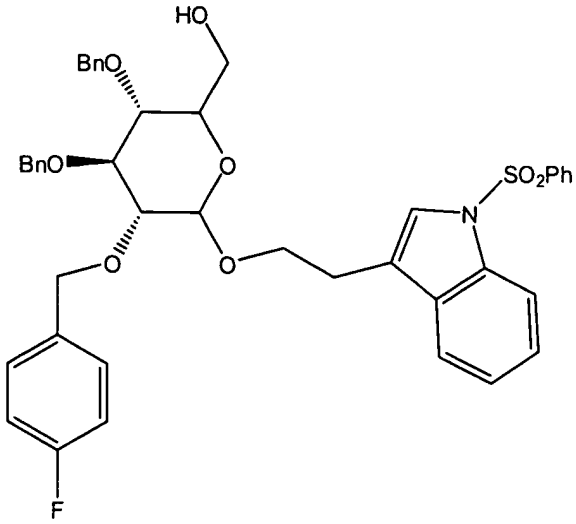
Example 85 compound IV-81



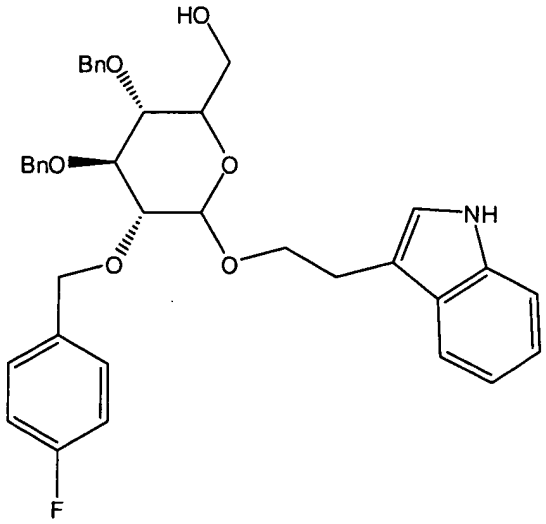
Example 86 compound IV-82



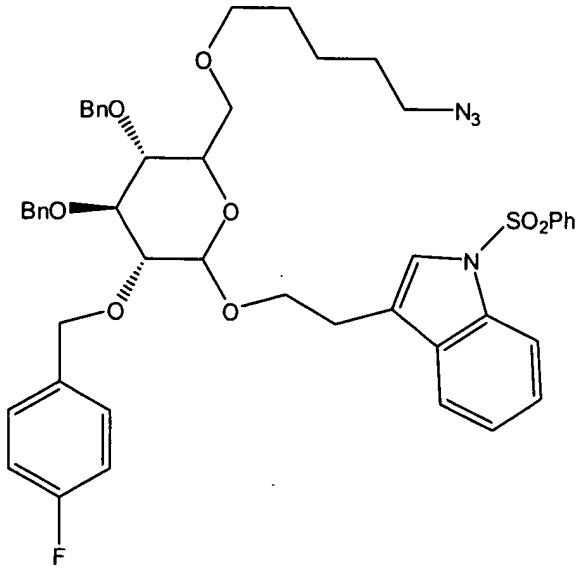
Example 87 compound IV-83



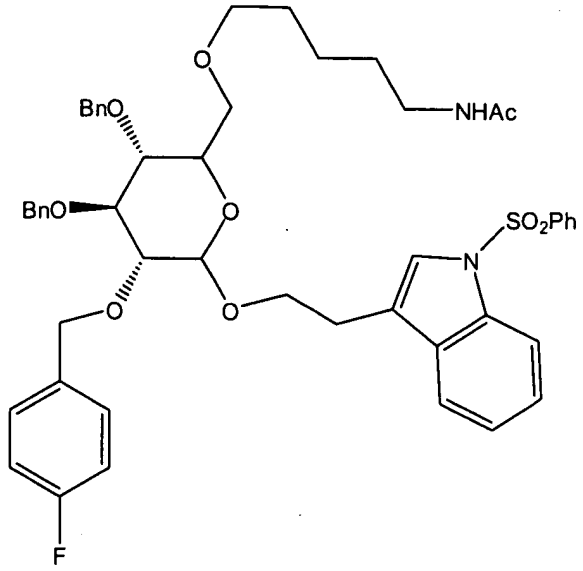
Example 88 compound IV-84



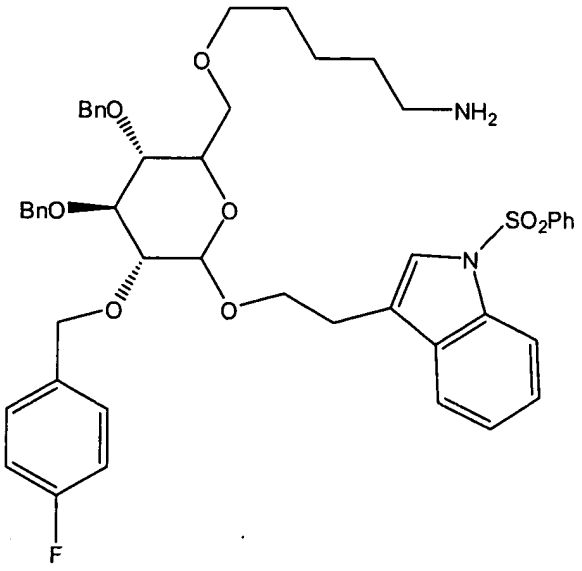
Example 89 compound IV-85



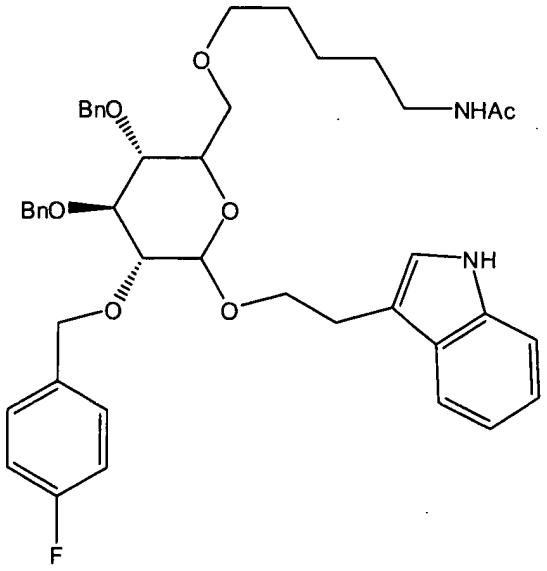
Example 91 compound IV-87



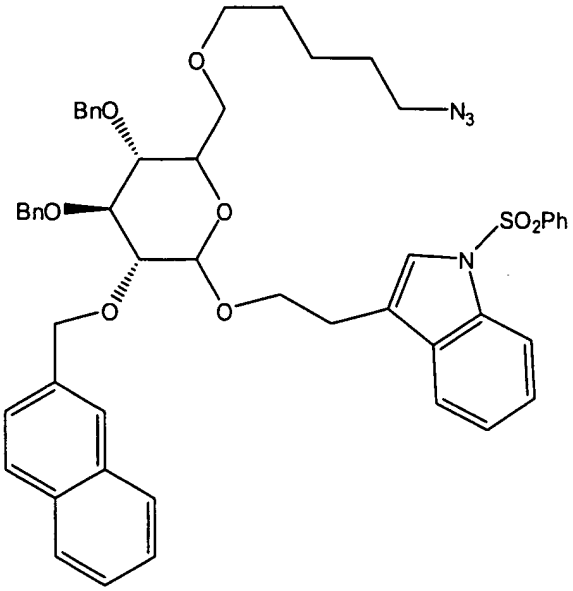
Example 90 compound IV-86



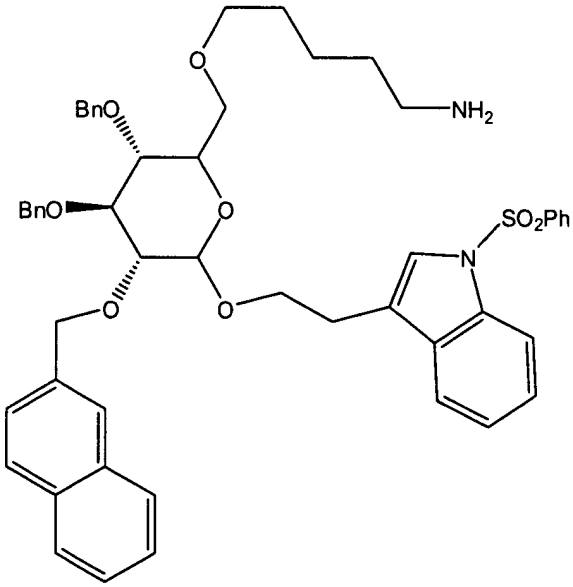
Example 92 compound IV-88



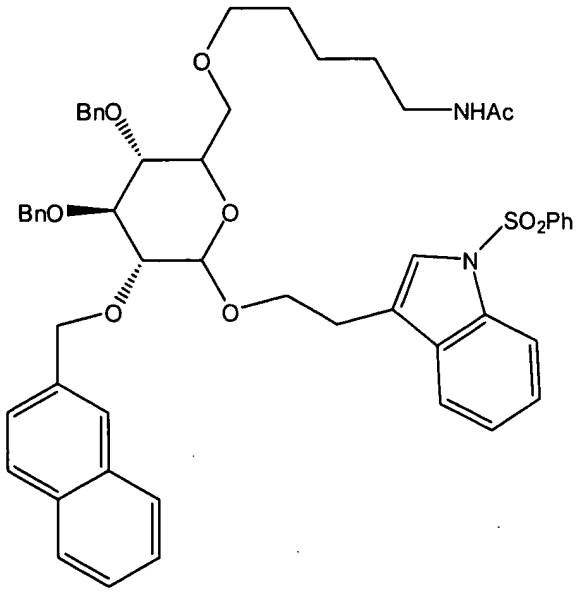
Example 93 compound IV-89



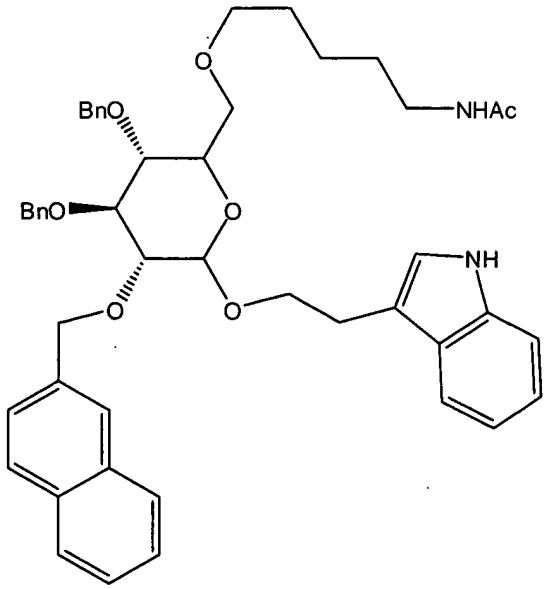
Example 94 compound IV-90



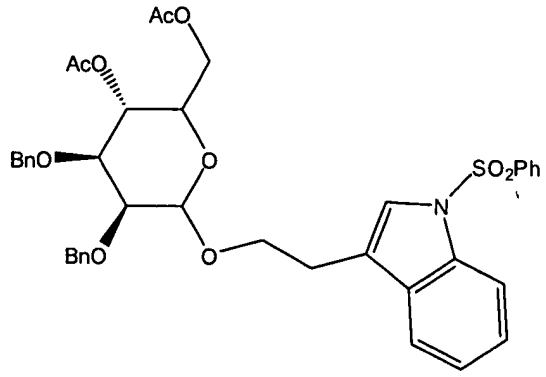
Example 95 compound IV-91



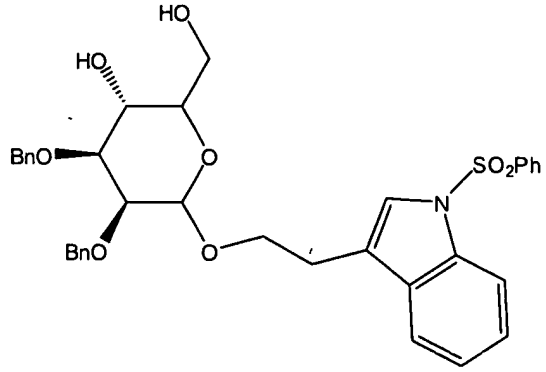
Example 96 compound IV-92



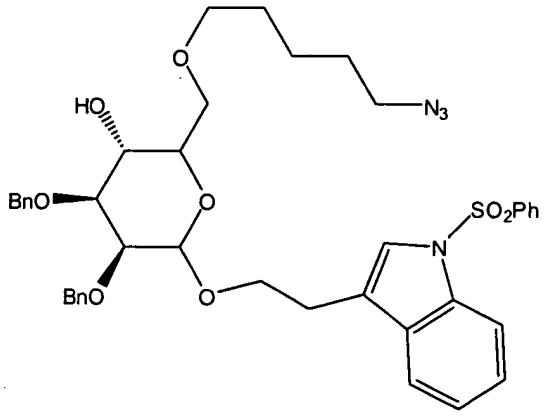
Example 97 compound IV-94



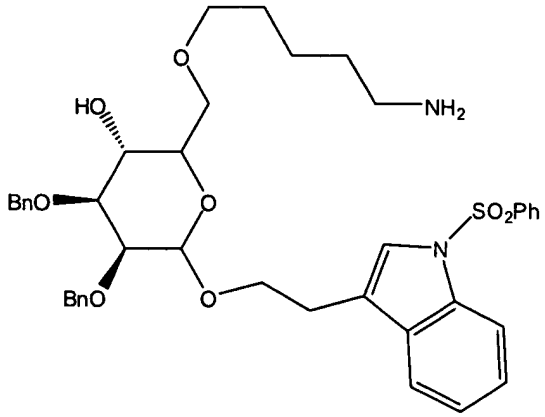
Example 98 compound IV-95



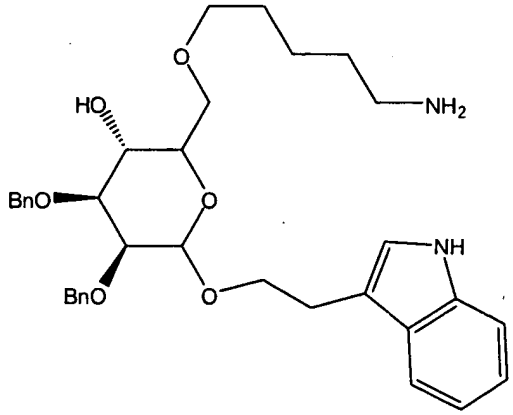
Example 99 compound IV-96



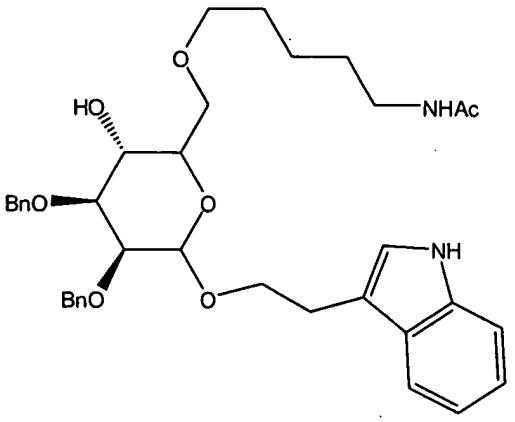
Example 100 compound IV-97



Example 101 compound IV-98

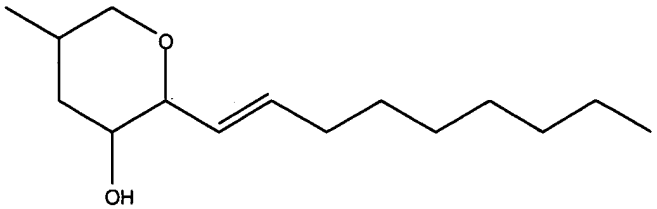


Example 102 compound IV-99

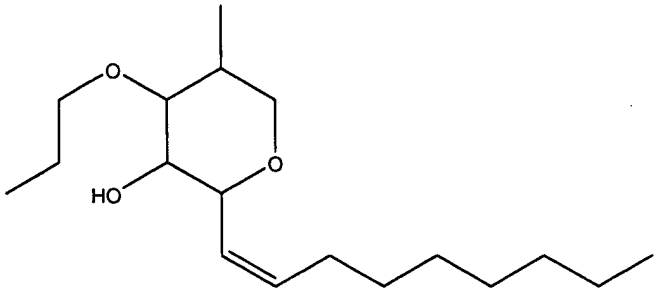


ATTACHMENT II

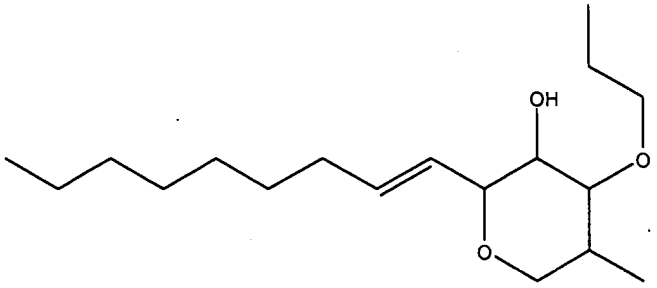
Compounds of page 4 line 50 to page 7 line 4 are relevant to the present discussion.



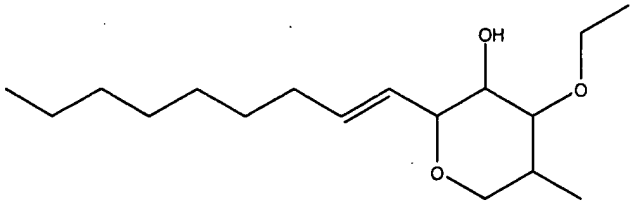
5-methyl-2-[(E)-1-nonenyl]tetrahydro-2H-pyran-3-ol



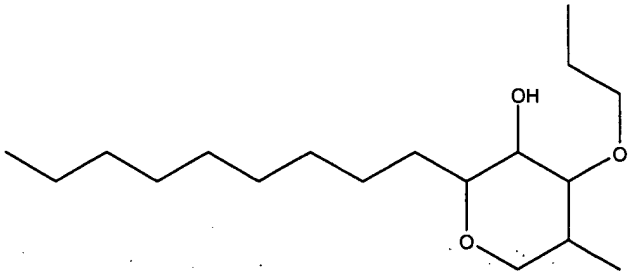
5-methyl-2-[(Z)-1-nonenyl]-4-propoxytetrahydro-2H-pyran-3-ol



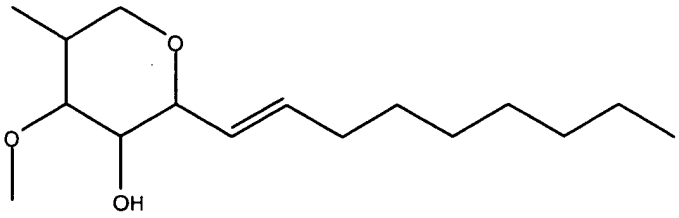
5-methyl-2-[(E)-1-nonenyl]-4-propoxytetrahydro-2H-pyran-3-ol



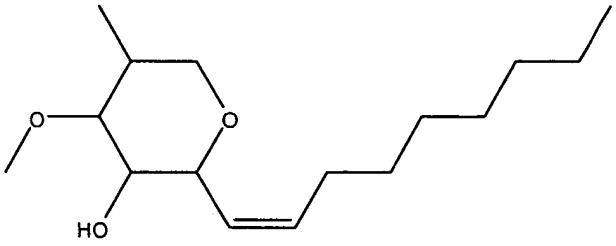
4-ethoxy-5-methyl-2-[(E)-1-nonenyl]tetrahydro-2H-pyran-3-ol



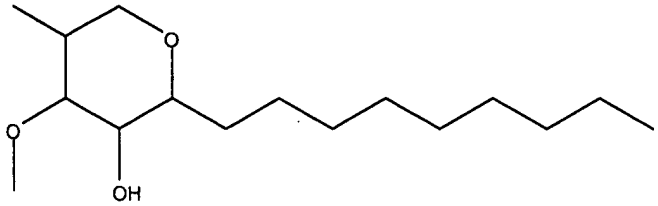
5-methyl-2-nonyl-4-propoxytetrahydro-2H-pyran-3-ol



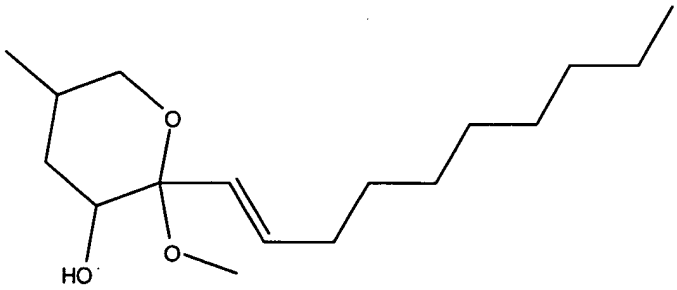
4-methoxy-5-methyl-2-[(E)-1-nonenyl]-tetrahydro-2H-pyran-3-ol



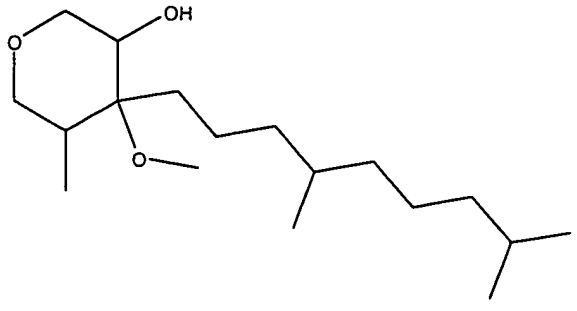
4-methoxy-5-methyl-2-[(Z)-1-nonenyl]-tetrahydro-2H-pyran-3-ol



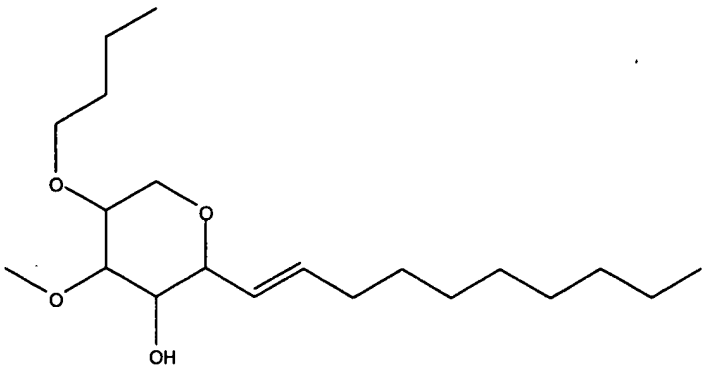
4-methoxy-5-methyl-2-nonyl-tetrahydro-2H-pyran-3-ol



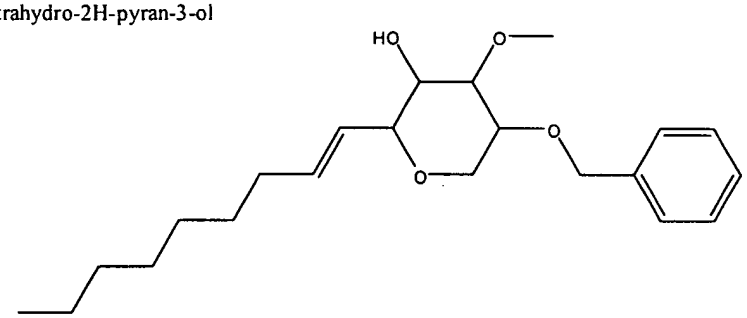
2-methoxy-5-methyl-[(E)-decenyl]-tetrahydro-2H-pyran-3-ol



4-(4,8-dimethylnonyl)-4-methoxy-5-methyl-tetrahydro-2H-pyran-3-ol



5-butoxy-4-methoxy-2-[(E)decenyl]tetrahydro-2H-pyran-3-ol



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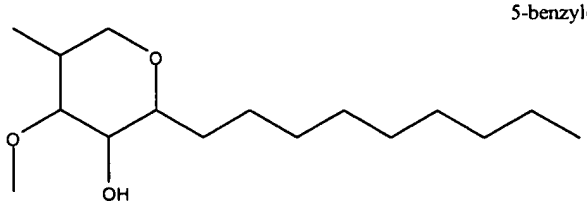

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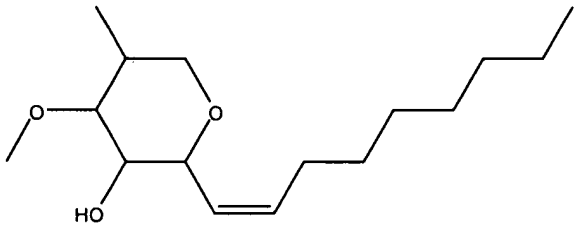

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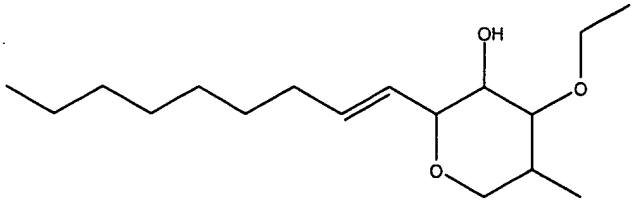
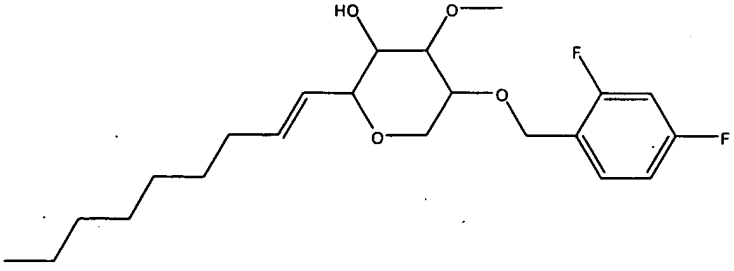
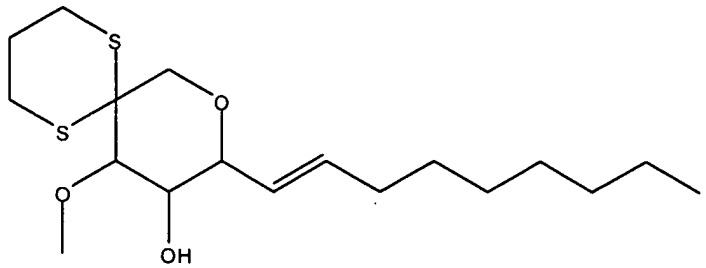


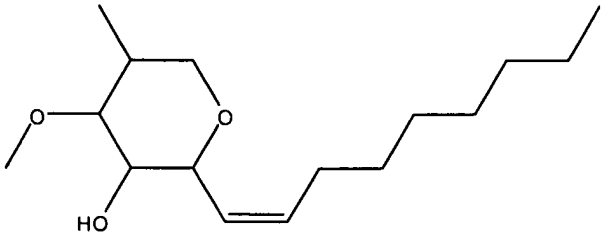
4-ethoxy-5-methyl-2-[(E)-1-nonenyl]-tetrahydro-2H-pyran-3-ol



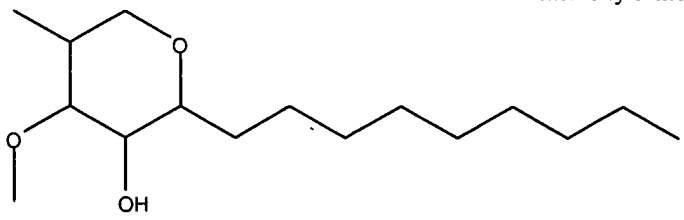
5-(2,4-difluorobenzyloxy)-4-methoxy-2-[(E)-1-nonenyl]-tetrahydro-2H-pyran-3-ol



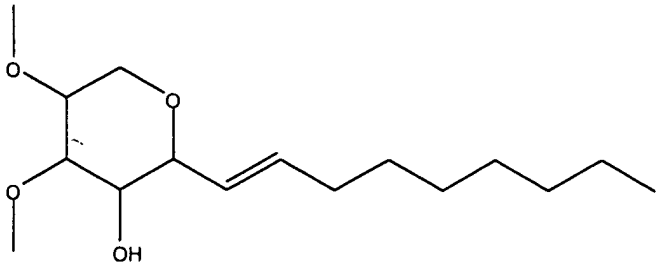
11-methoxy-9-[(e)-1-nonenyl]-8-oxa-1,5-dithispiro-[5,5]undecan-10-ol



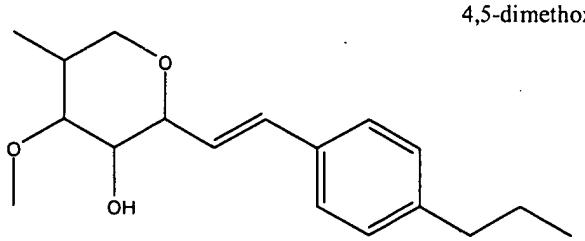
4-methoxy-5-methyl-2-[(Z)-1-nonenyl]tetrahydro-2H-pyran-3-ol



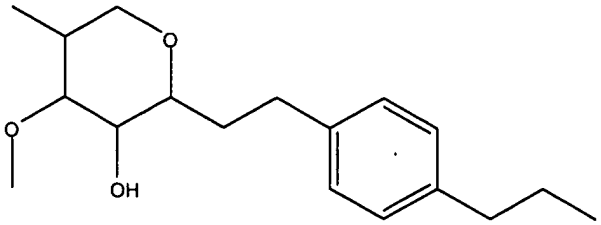
4-methoxy-5-methyl-2-nonyltetrahydro-2H-pyran-3-ol



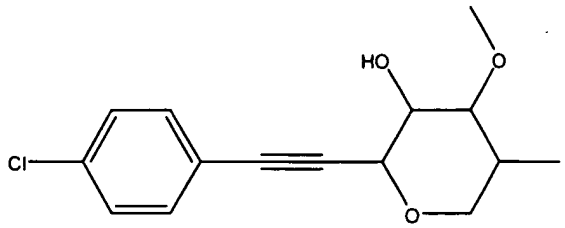
4,5-dimethoxy-2-[(E)-1-nonenyl]tetrahydro-2H-pyran-3-ol



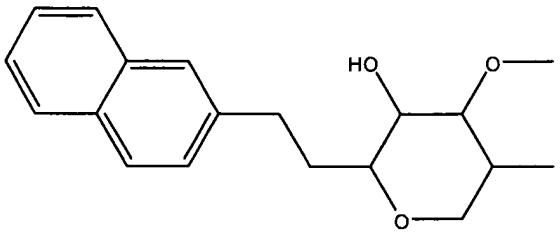
4-methoxy-5-methyl-2-[(E)-2-(4-propylphenyl)-vinyl]tetrahydro-2H-pyran-3-ol



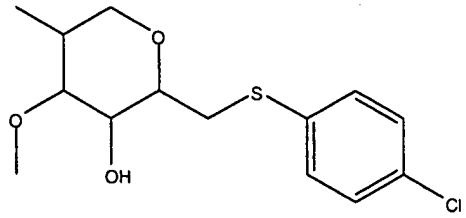
4-methoxy-5-methyl-2-[(E)-2-(4-propylphenyl)ethyl]tetrahydro-2H-pyran-3-ol



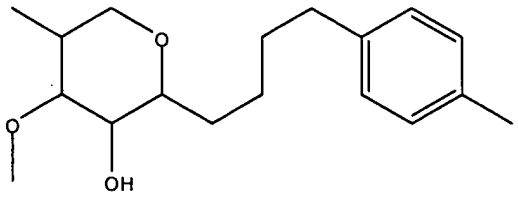
2-[2-(4-chlorophenyl)ethynyl]-4-methoxy-5-methyltetrahydro-2H-pyran-3-ol



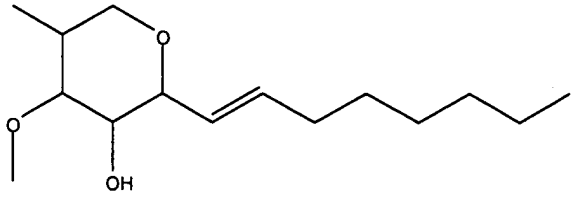
4-methoxy-5-methyl-2-(2-naphthylethyl)tetrahydro-2H-pyran-3-ol



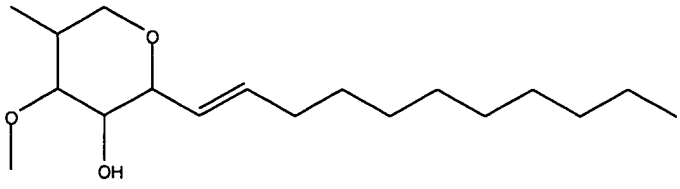
2-[(4-chlorophenylthio)methyl]-4-methoxy-5-methyltetrahydro-2H-pyran-3-ol



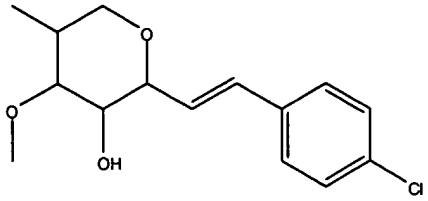
4-methoxy-5-methyl-2-[4-(4-methylphenyl)butyl]tetrahydro-2H-pyran-3-ol



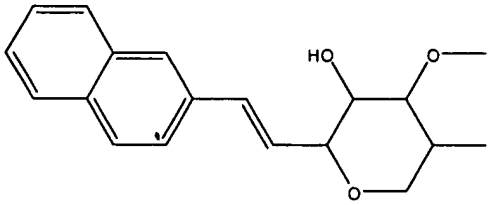
4-methoxy-5-methyl-2-[(E)-1-octenyl]tetrahydro-2H-pyran-3-ol



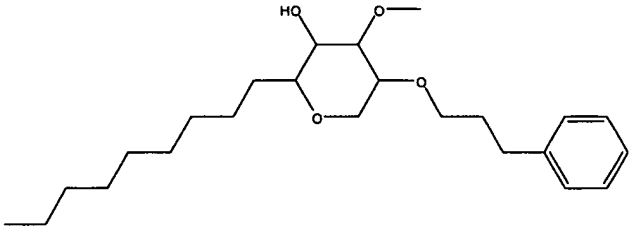
4-methoxy-5-methyl-2-[(E)-1-undecenyl]tetrahydro-2H-pyran-3-ol



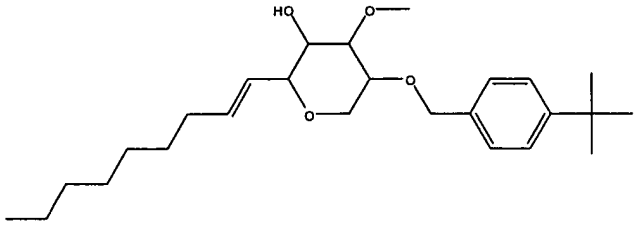
2-[(E)-2-(4-chlorophenyl)vinyl]-4-methoxy-5-methyltetrahydro-2H-pyran-3-ol



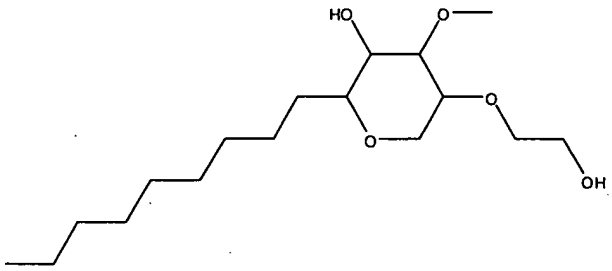
4-methoxy-5-methyl-2-[(E)-2-(2-naphthyl)-vinyl]-tetrahydro-2H-pyran-3-ol



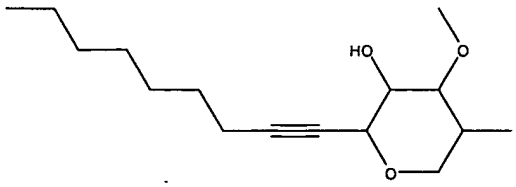
4-methoxy-2-nonyl-5-(3-phenylpropoxy)-tetrahydro-2H-pyran-3-ol



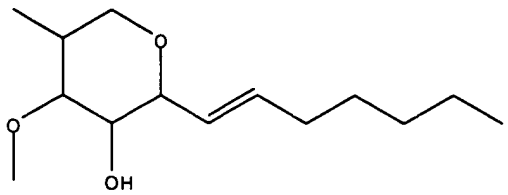
5-(4-tertbutylbenzyloxy)-4-methoxy-2-[(E)-1-nonenyl]tetrahydro-2H-pyran-3-ol



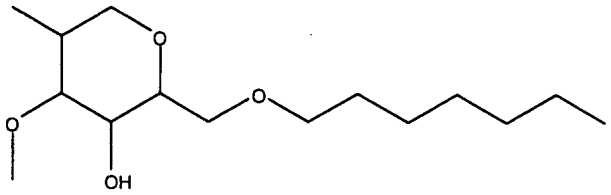
5-(2-hydroxyethoxy)-4-methoxy-2-nonyl-tetrahydro-2H-pyran-3-ol



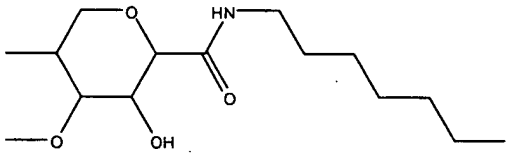
4-methoxy-5-methyl-2-(1-nonynyl)-tetrahydro-2H-pyran-3-ol



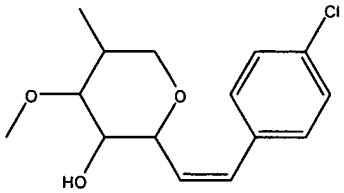
4-methoxy-5-methyl-2-[(E)-1-heptenyl]-tetrahydro-2H-pyran-3-ol



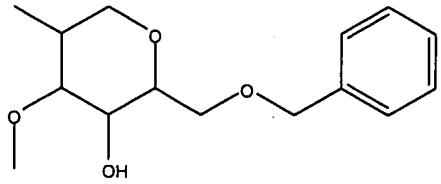
2-(heptyloxymethyl)-4-methoxy-5-methyl-tetrahydro-2H-pyran-3-ol



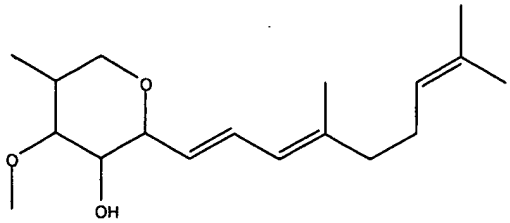
N-heptyl-3-hydroxy-4-methoxy-5-methyltetrahydro-2H-pyran-2-carboxamide



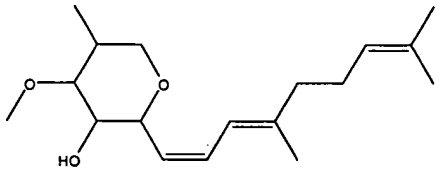
2-[(Z)-2-(4-chlorophenyl)vinyl]-4-methoxy-5-methyltetrahydro-2H-pyran-3-ol



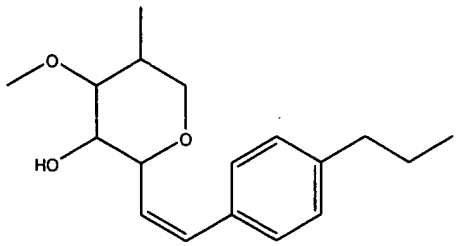
2-benzyloxymethyl-4-methoxy-5-methyltetrahydro-2H-pyran-3-ol



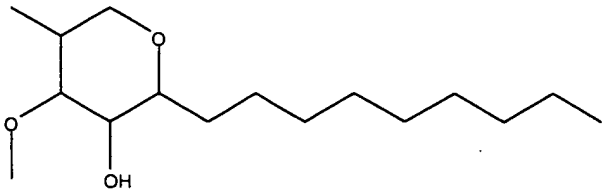
2-[(1E,3E)-4,8-dimethyl-1,3,7-nonatrienyl]-4-methoxy-5-methyltetrahydro-2H-pyran-3-ol



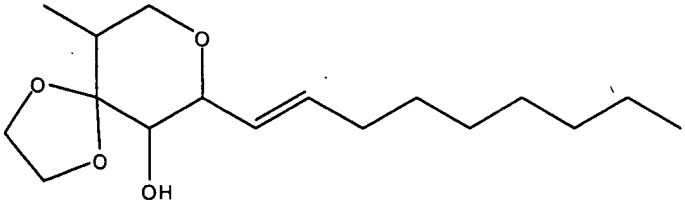
2-[(1Z,3E)-4,8-dimethyl-1,3,7-nonatrienyl]-4-methoxy-5-methyltetrahydro-2H-pyran-3-ol



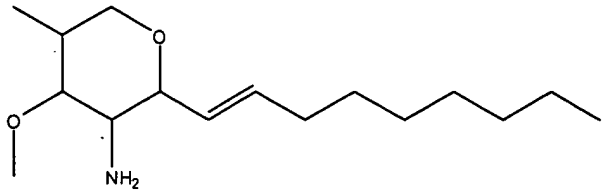
2-[(Z)-2-(4-propylphenyl)vinyl]-4-methoxy-5-methyltetrahydro-2H-pyran-3-ol



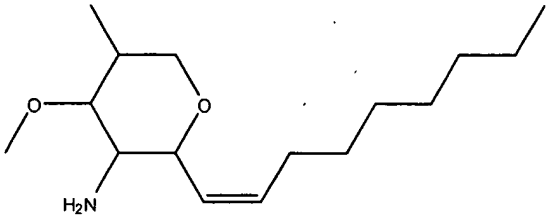
2-nonyl-4-methoxy-5-methyltetrahydro-2H-pyran-3-ol



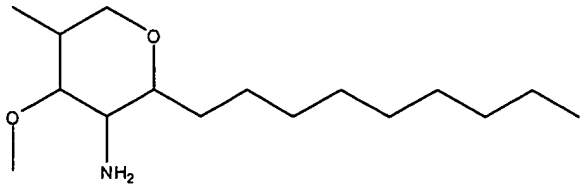
10-methyl-7-[(E)-1-nonenyl]-1,4,8-trioxaspiro[4,5]decan-6-ol



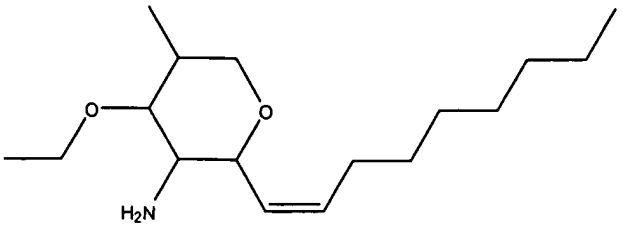
4-methoxy-5-methyl-2-[(E)-1-nonenyl]tetrahydro-2H-pyran-3-amine



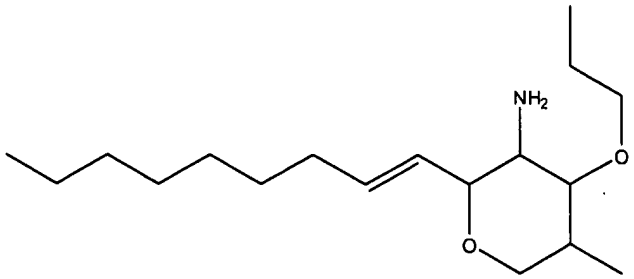
4-methoxy-5-methyl-2-[(Z)-1-nonenyl]tetrahydro-2H-pyran-3-amine



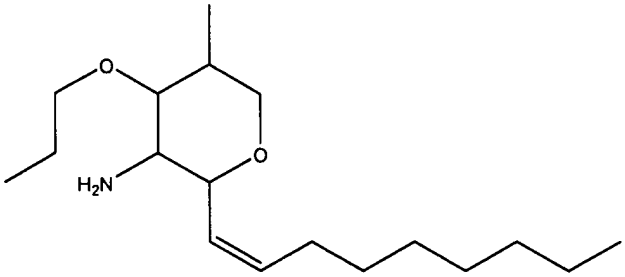
4-methoxy-5-methyl-2-nonyl-tetrahydro-2H-pyran-3-amine



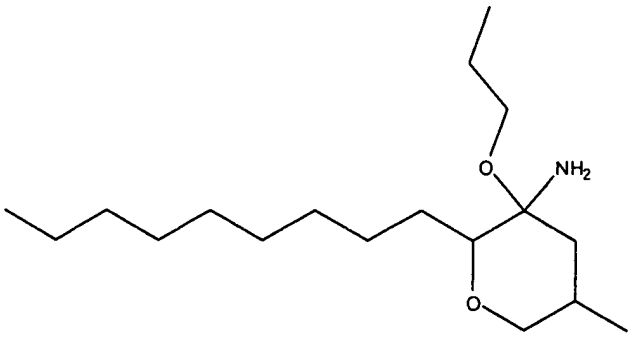
4-ethoxy-5-methyl-2-[(Z)-1-nonenyl]tetrahydro-2H-pyran-3-amine



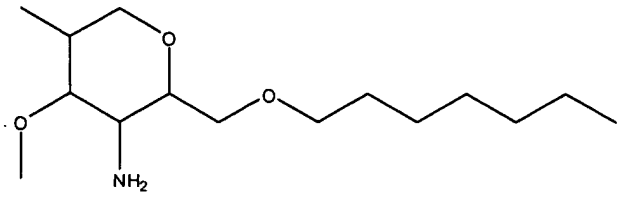
4-propoxy-5-methyl-2-[(E)-1-nonenyl]tetrahydro-2H-pyran-3-amine



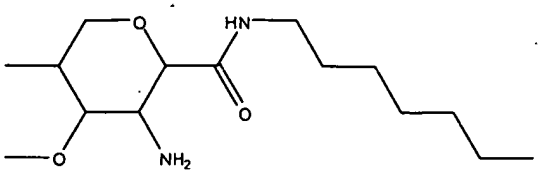
4-propoxy-5-methyl-2-[(Z)-1-nonenyl]tetrahydro-2H-pyran-3-amine



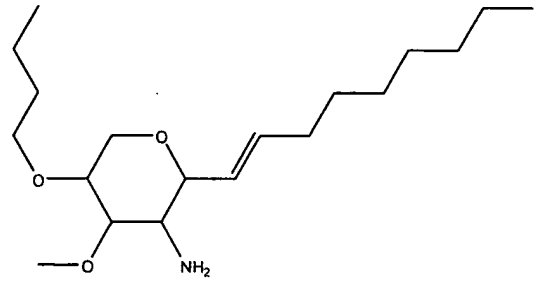
3-propoxy-5-methyl-2-nonyl-tetrahydro-2H-pyran-3-amine



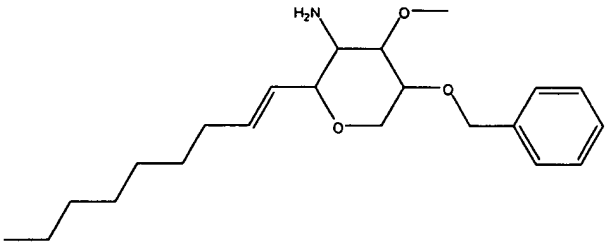
4-methoxy-5-methyl-2-heptyloxymethyl-tetrahydro-2H-pyran-3-amine



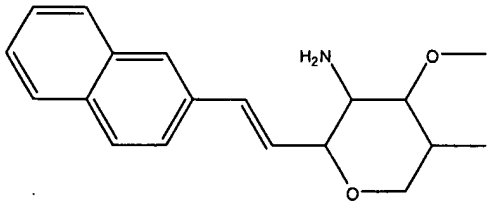
3-amino-N-heptyl-4-methoxy-5-methyl-tetrahydro-2H-pyran-2-carboxamide



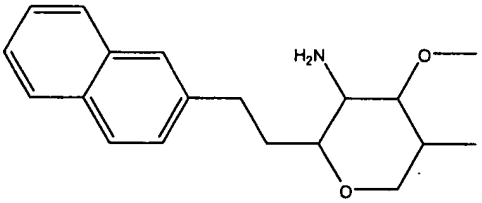
4-methoxy-5-butoxy-2-[(E)-1-nonenyl]-tetrahydro-2H-pyran-3-amine



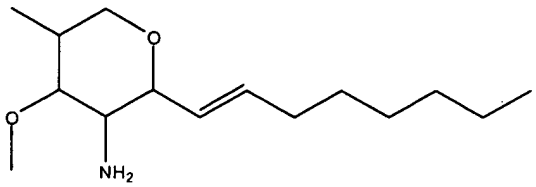
4-methoxy-5-benzyloxy-2-[(E)-1-nonenyl]-tetrahydro-2H-pyran-3-amine



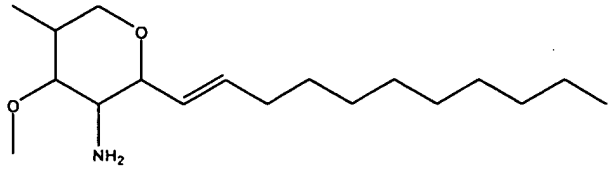
4-methoxy-5-methyl-2-[(E)-2-(2-naphthyl)vinyl]-tetrahydro-2H-pyran-3-amine



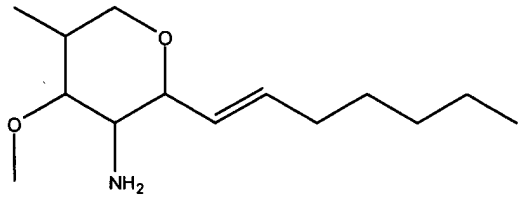
4-methoxy-5-methyl-2-(2-naphthyl)ethyl-tetrahydro-2H-pyran-3-amine



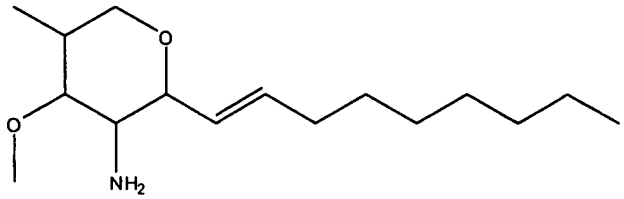
4-methoxy-5-methyl-2-[(E)-1-octenyl]-tetrahydro-2H-pyran-3-amine



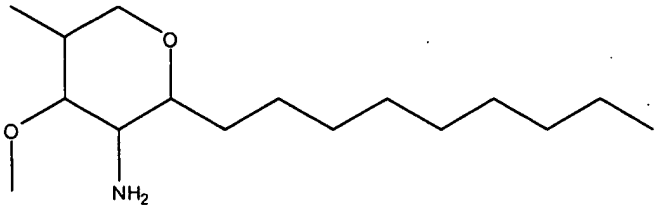
4-methoxy-5-methyl-2-[(E)-1-undecenyl]-tetrahydro-2H-pyran-3-amine



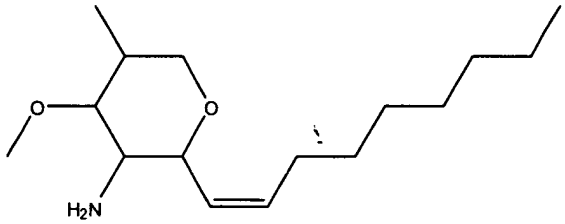
4-methoxy-5-methyl-2-[(E)-1-heptenyl]-tetrahydro-2H-pyran-3-amine



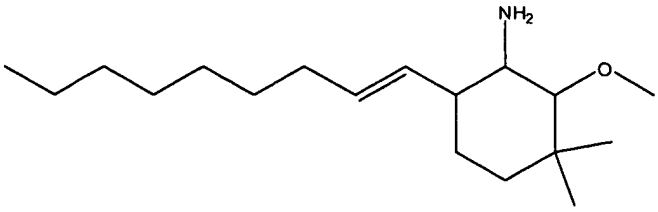
4-methoxy-5-methyl-2-[(E)-1-nonenyl]-tetrahydro-2H-pyran-3-amine



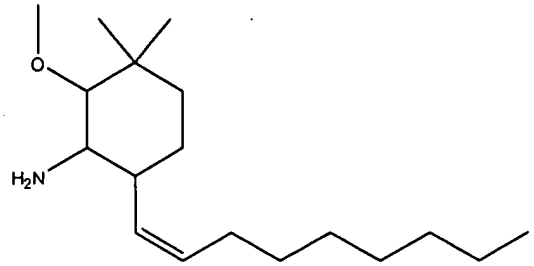
4-methoxy-5-methyl-2-nonyl-tetrahydro-2H-pyran-3-amine



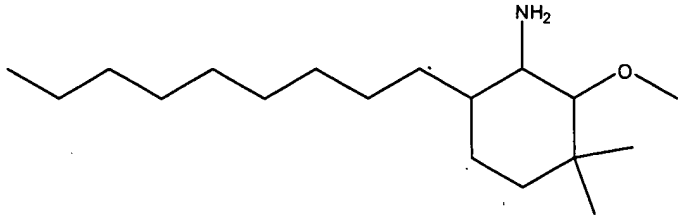
4-methoxy-5-methyl-2-[(Z)-1-nonenyl]-tetrahydro-2H-pyran-3-amine



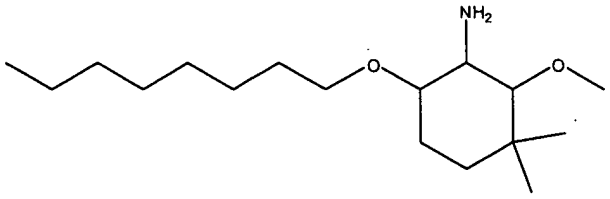
[2methoxy-3,3-dimethyl-6-[(E)-1-nonenyl]cyclohexyl]amine



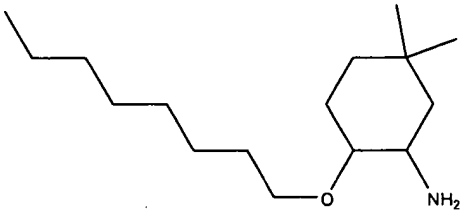
[2methoxy-3,3-dimethyl-6-[(Z)-1-nonenyl]cyclohexyl]amine



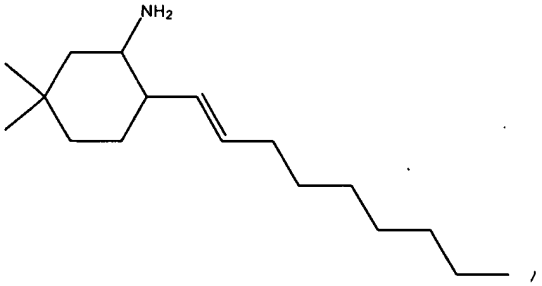
[2methoxy-3,3-dimethyl-6-nonyl-cyclohexyl]amine



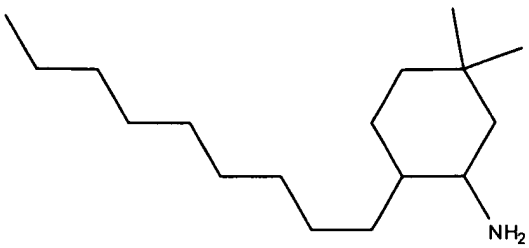
[2-methoxy-3,3-dimethyl-6-octyloxy-cyclohexyl]amine



[5,5-dimethyl-2-octyloxy-cyclohexyl]amine



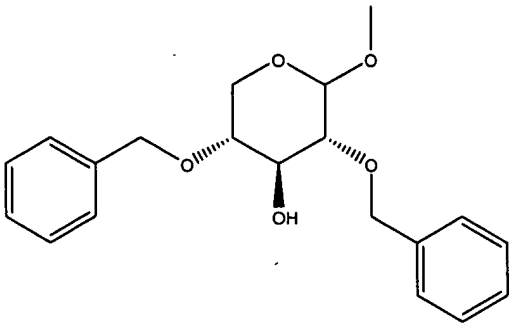
[5,5-dimethyl-2-[(E)-1-nonenyl]-cyclohexyl]amine



[5,5-dimethyl-2-nonyl-cyclohexyl]amine

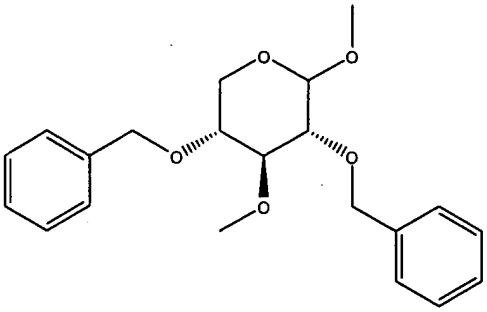
From page 22 line 60 to page 38 line 55 a number of reference examples are described. Those compounds not described in the list above are indicated below.

1a



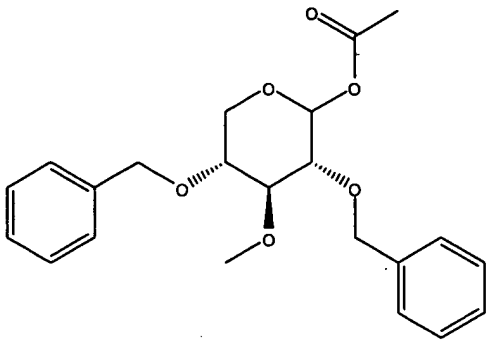
methyl 2,4-di-O-benzyl-xylopyranoside

1b



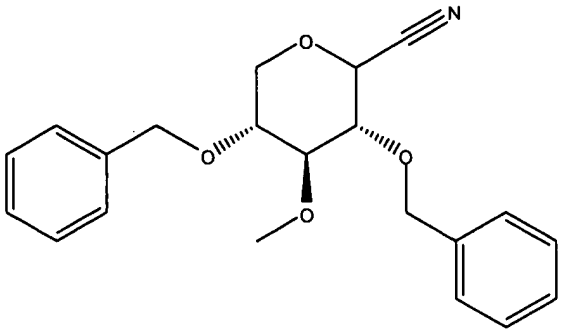
methyl 3-O-methyl-2,4-di-O-benzyl-xylopyranoside

1c



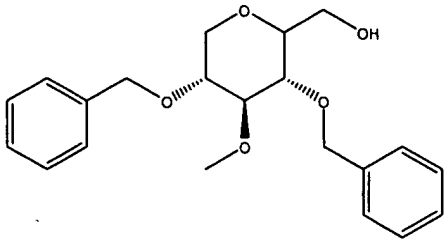
3-O-methyl-2,4-di-O-benzyl-xylopyranosyl acetate

1d



3-O-methyl-2,4-di-O-benzyl-xylopyranosyl cyanide

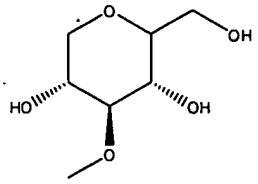
1e



3-O-methyl-2,4-di-O-benzyl-1,5-anhydroglucitol

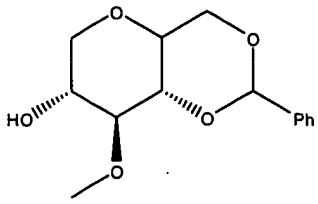
((3*S*,4*S*,5*R*)-3,5-bis(benzyloxy)-4-methoxytetrahydro-2*H*-pyran-2-yl)methanol

1f



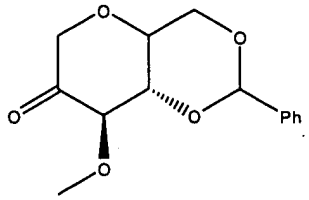
(3*S*,4*S*,5*R*)-2-(hydroxymethyl)-4-methoxytetrahydro-2*H*-pyran-3,5-diol

1g



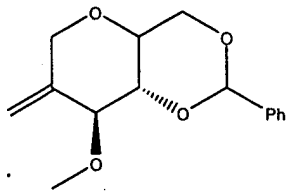
(7*R*,8*S*,8a*S*)-8-methoxy-2-phenylhexahydropyrano[3,2-*d*][1,3]dioxin-7-ol

1h



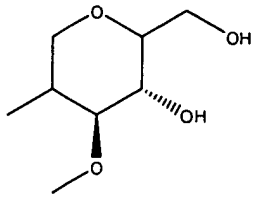
(8*R*,8a*S*)-8-methoxy-2-phenyltetrahydropyrano[3,2-*d*][1,3]dioxin-7(6*H*)-one

1i



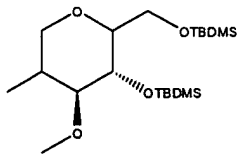
(8*S*,8a*R*)-8-methoxy-7-methylene-2-phenylhexahydropyrano[3,2-*d*][1,3]dioxine

1j



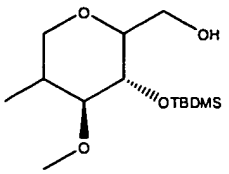
(3*R*,4*S*)-2-(hydroxymethyl)-4-methoxy-5-methyltetrahydro-2*H*-pyran-3-ol

1k



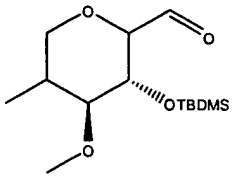
tert-butyl(((3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)methoxy)dimethylsilane

1l



((3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)methanol

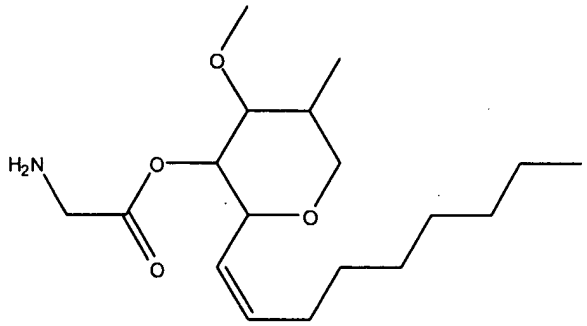
1m



(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-methoxy-5-methyltetrahydro-2*H*-pyran-2-carbaldehyde

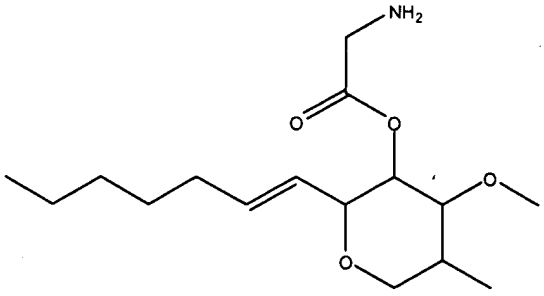
From page 39 line 55 to page 56 line 65 are described a number of worked examples. Those compounds not described above and for which X is oxygen are described below.

Example 1



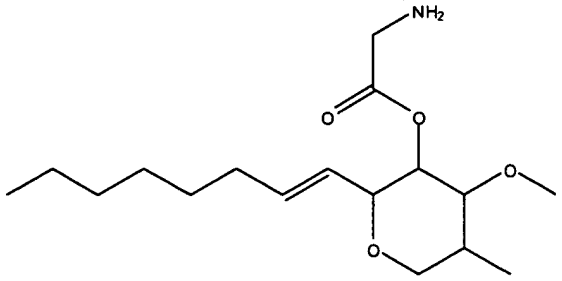
4-methoxy-5-methyl-2-[(Z)-1-nonenyl]tetrahydro-2H-pyran-3-yl glycinate

Example 2



4-methoxy-5-methyl-2-[(E)-1-heptenyl]tetrahydro-2H-pyran-3-yl glycinate

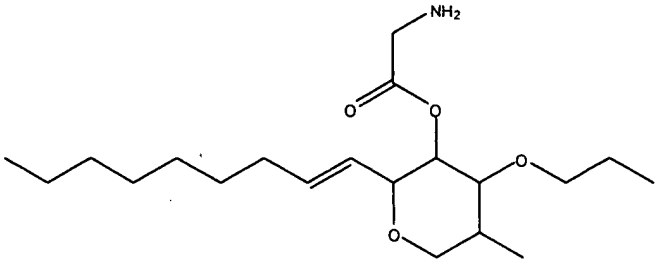
Example 3



4-methoxy-5-methyl-2-[(E)-1-octenyl]tetrahydro-2H-pyran-3-yl glycinate

Example 4 – Example 20 are analogues of example 3 varying either in stereochemistry or the chain appended at position 2.

Example 21

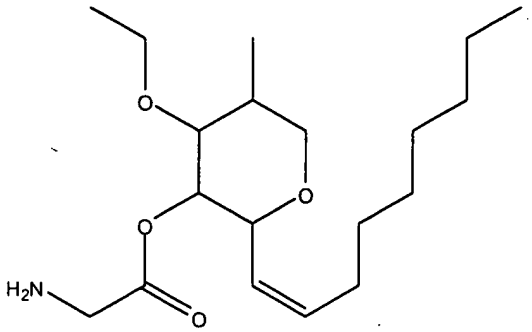


4-propoxy-5-methyl-2-[(E)-1-nonenyl]tetrahydro-2H-pyran-3-yl glycinate

Example 22 and 23 are analogues of example 21.

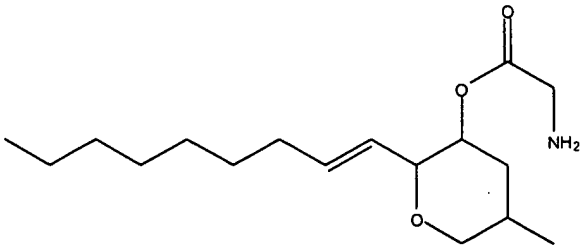
Example 24 to Example 26 are analogues of Example 4

Example 27



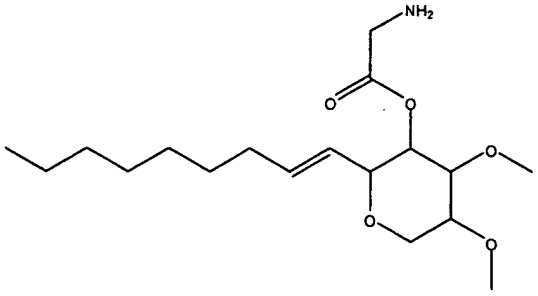
4-ethoxy-5-methyl-2-[(Z)-1-nonenyl]tetrahydro-2H-pyran-3-yl glycinate

Example 28



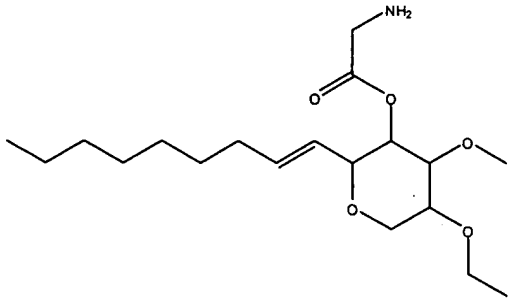
5-methyl-2-[(E)-1-nonenyl]tetrahydro-2H-pyran-3-yl glycinate

Example 29



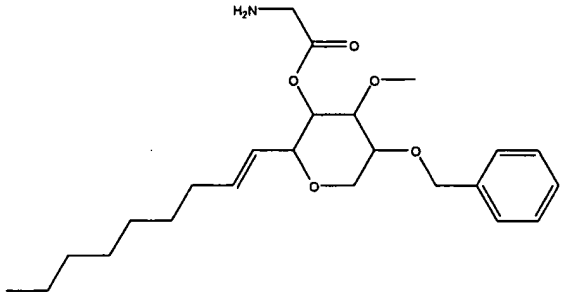
4,5-dimethoxy-2-[(E)-1-nonenyl]tetrahydro-2H-pyran-3-yl glycinate

Example 30



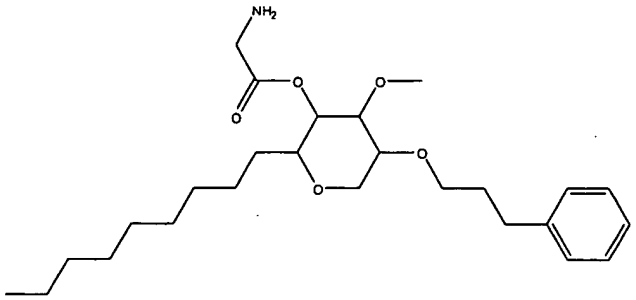
5-ethoxy-4-methoxy-2-[(E)-1-nonenyl]tetrahydro-2H-pyran-3-yl glycinate

Example 31



5-benzyloxy-4-methoxy-2-[(E)-1-nonenyl]tetrahydro-2H-pyran-3-yl glycinate

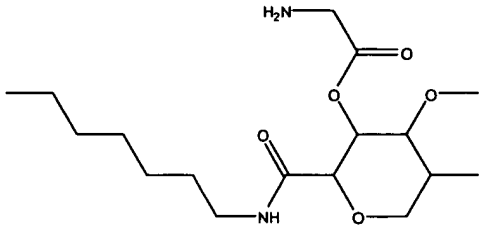
Example 32



5-(3-phenylpropoxy)-4-methoxy-2-nonyl-tetrahydro-2H-pyran-3-yl glycinate

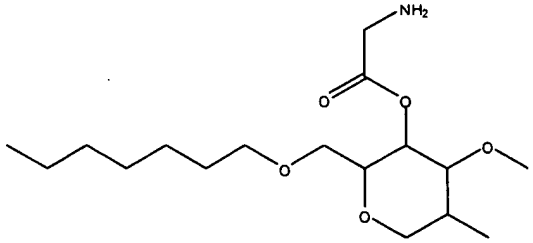
Example 33 to Example 39 are analogues of Example 31 or 32.

Example 40



2-heptylcarbamoyl-4-methoxy-5-methyl-tetrahydro-2H-pyran-3-yl glycinate

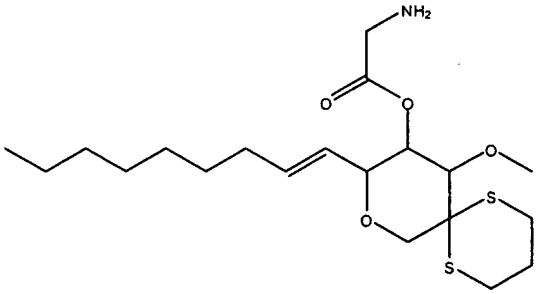
Example 41



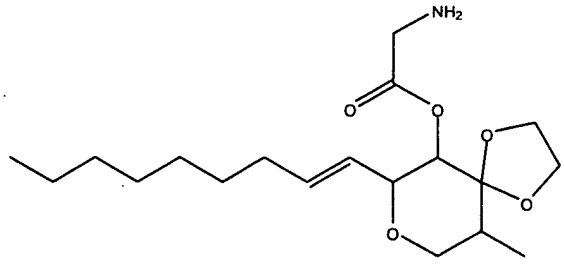
2-heptoxymethyl-4-methoxy-5-methyl-tetrahydro-2H-pyran-3-yl glycinate

Example 42 to Example 44 are analogues of example 31

Example 45

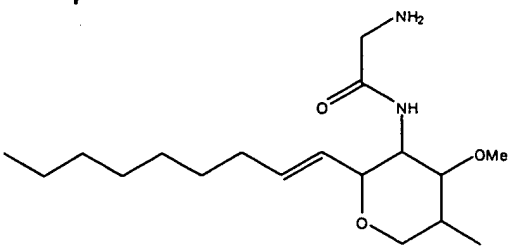


Example 46



Example 47 to 51 are analogues of 31 and 32

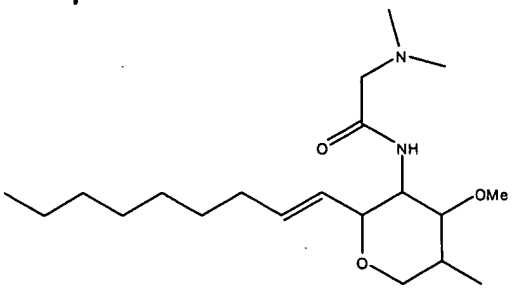
Example 52



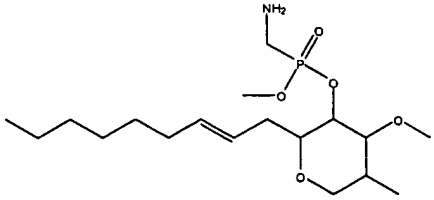
Example 53 is an analogue of 52

Example 54 to example 55 relate to cyclohexane based molecules

Example 56

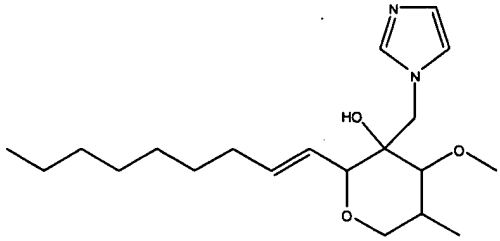


Example 57



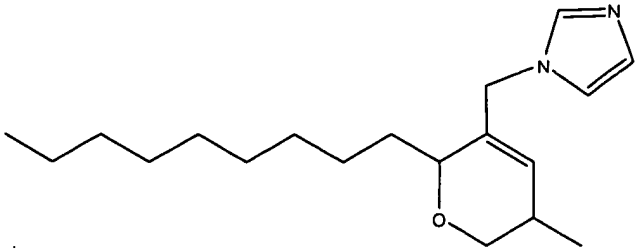
2-nonenyl-4-methoxy-5-methyl-tetrahydro-2H-pyran-3-yl methyl aminomethylphosphonate

Example 58



(*E*)-3-((1*H*-imidazol-1-yl)methyl)-4-methoxy-5-methyl-2-(non-1-enyl)tetrahydro-2*H*-pyran-3-ol

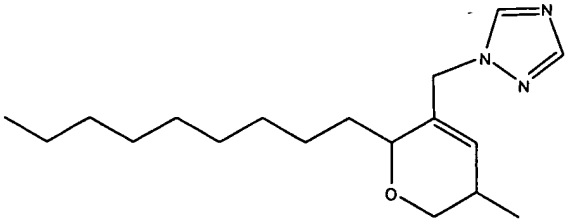
Example 59



1-((5-methyl-2-nonyl-5,6-dihydro-2*H*-pyran-3-yl)methyl)-1*H*-imidazole

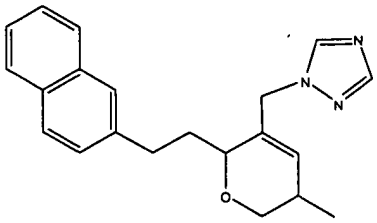
Example 60 = Same as 59

Example 61



1-((5-methyl-2-nonyl-5,6-dihydro-2*H*-pyran-3-yl)methyl)-1*H*-1,2,4-triazole

Example 62



1-((5-methyl-2-(2-(naphthalen-2-yl)ethyl)-5,6-dihydro-2*H*-pyran-3-yl)methyl)-1*H*-1,2,4-triazole

Examples from 63 to the end are concerned with cyclohexane based molecules.